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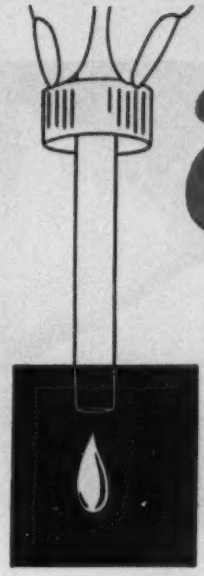

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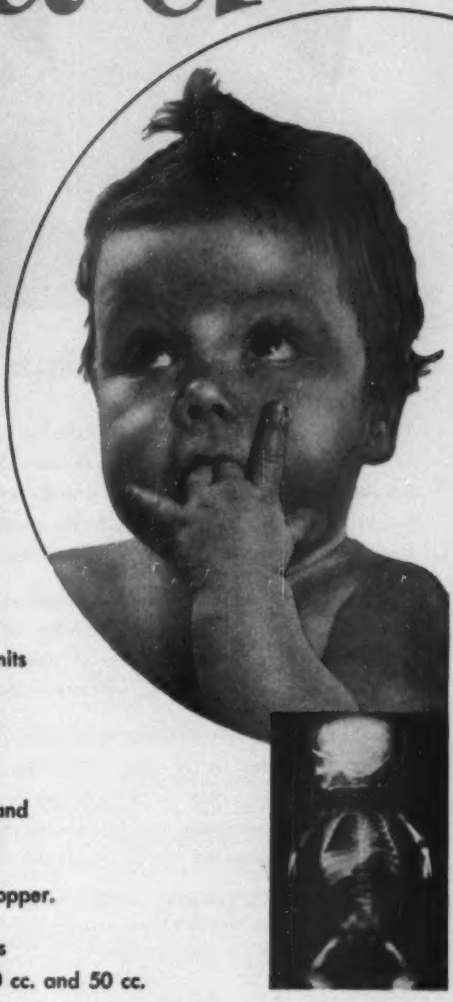

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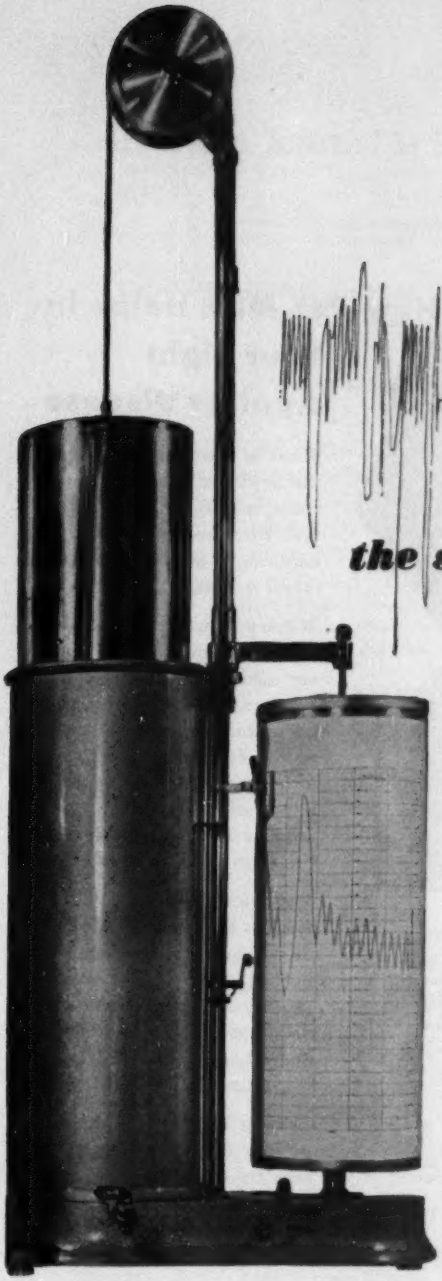

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EXCHANGE TRANSFUSION IN ERYTHROBLASTOSIS FETALIS AND OTHER CONDITIONS

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BROOKLYN

THE PURPOSE of this communication is to describe some experiences of my colleagues and me with the use of exchange transfusion. In our series of 26 exchange transfusions, 24 were performed for the treatment of erythroblastosis fetalis due to Rh sensitization and 2 for other conditions, which will be described later in this paper. This series

TABLE 1.—*Cases Without Abnormal Obstetric History and/or History of Blood Transfusion*

Case No.	Patient's Blood Type	Pregnancy No.	Maternal Rh Antibody Titer *	Result
4	O Rh₁rh	2	32 congl.	Recovered
5	A Rh₁rh	2 †	24 aggl. & congl.	Recovered
7	O Rh₁rh	4	8 congl.	Recovered
8	B Rh₁rh	2	8 congl.	Recovered
10	O Rh₁rh	2	16 aggl. 24 congl.	Recovered
15	A Rh₁rh	2	0 aggl. 8 congl.	Recovered
17	B Rh₁rh	2	4 congl.	Recovered
21	A Rh₁rh	2	48 congl.	Recovered
22	O Rh₁rh	2	48 congl.	Recovered
23	O Rh₁rh	1	48 congl.	Recovered

* Aggl. indicates agglutination method; congl., conglutination (albumin-plasma) method. 5. (Wiener, A. S., and Hurst, J. G.: Exper. Med. & Surg. 5 : 295, 1947).

† Cesarean section was done five weeks before term.

exhibits several interesting features which will be pointed out in the discussion of the cases.

The 24 cases of erythroblastosis have been divided into four classes: (1) those without an abnormal obstetric history and/or history of blood transfusion (table 1); (2) those with an abnormal obstetric history and/or history of blood transfusion (table 2); (3) those with a history of erythroblastosis with recovery (table 3), and (4) those with a history of fatal erythroblastosis (table 4).

As would be expected, the highest mortality occurred in the last category, in which there were 2 cases and both patients died. In 1 of these autopsy disclosed hemorrhage into the ventricles, whereas in the

TABLE 2.—*Cases with Abnormal Obstetric History and/or History of Blood Transfusion*

Case No.	Clinical History	Patient's Blood Type	Pregnancy No.	Maternal Rh Antibody Titer *	Result
9	Third baby delivered at 7 mo. (anencephalic)	A Rh₁rh	4	12 aggl. & congl.	Recovered
6	Three miscarriages, at 3, 5 and 6½ mo.	A Rho	4	8 congl.	Recovered
11	Second pregnancy resulted in stillbirth; fetal heart heard 2 wk. before delivery	A Rh₁rh	3 †	8 congl.	Died during transfusion
13	Spontaneous abortion at 3½ mo. in second pregnancy	O Rh₁rh	3	24 aggl. 32 congl.	Recovered
14	Spontaneous abortion at 3 mo. in third pregnancy	O Rh₁rh	4	16 aggl. 16 congl.	Recovered
20	Two transfusions about 9 yr. previously, reaction after 2d.; cesarean section 1 mo. before term (first pregnancy)	A Rh₁rh	1 ‡	16 congl.	Died; intracranial hemorrhage noted at autopsy

* Aggl. indicates agglutination method; congl., conglutination (albumin-plasma) method.
† Abortion induced at 35 weeks.
‡ Cesarean section one month before term.

TABLE 3.—*Cases with History of Erythroblastosis with Recovery*

Case No.	Clinical History	Patient's Blood Type	Pregnancy No.	Maternal Rh Antibody Titer *	Result
1	Second baby given 5 small transfusions before recovery	A Rh₁rh	3	Not determined	Recovered
12	Third child pallid and icteric at birth; did not develop normally; died at 9 mo. of pneumonia	O Rh₁rh	4	16 aggl. 24 congl.	Recovered †
16	Second child icteric at birth and given several small transfusions; jaundice lasted about 6 mo.; baby now apparently normal	O Rh₁rh	3	6 aggl. 24 congl.	Recovered
24	Second and third children treated with multiple small transfusions; both normal now	O Rh₁rh	4	48 congl.	Recovered
25	This baby is a sibling of the baby in case 6	A Rh₁rh	3	32 congl.	Recovered

* Aggl. indicates agglutination method; congl., conglutination (albumin-globulin) method.
† Icterus index 200 at start of transfusion.

other kernicterus developed in spite of a prompt exchange transfusion of 550 cc. of blood. Wiener and Wexler's reported mortality rate in this class is 41.2 per cent. The most favorable categories are 1 and 3, in which there was no mortality; Wiener and Wexler reported a mortality rate of 8.5 per cent and 0 per cent, respectively, for these classes. In class 2, our mortality rate is 33.3 per cent, as compared with 15.8 per cent of Wiener and Wexler. Intracranial hemorrhage was a complication in both of our patients in this class.

Our over-all mortality rate is 16.7 per cent and that of Wiener and Wexler 15.9 per cent. In table 5 our experiences with exchange transfusions are compared with those reported by other investigators.[1]

The importance of routine antepartum testing for Rh antibodies in the mother is brought out by our case 5. The patient, with group A,

TABLE 4.—*Cases with History of Erythroblastosis with Death*

Case No.	Clinical History	Patient's Blood Type	Pregnancy No.	Maternal Rh Antibody Titer *	Result
3	Second child treated with 2 small transfusions but died on 3d day of severe jaundice	A Rh_1rh	3	8 aggl.	Died on 3d day despite immediate exchange transfusion of 550 cc.; autopsy revealed kernicterus
9	Second child died on 2d day of severe icterus; received 2 small transfusions	B Rh_1rh	3	24 aggl. 32 congl.	Died shortly after completion of transfusion; autopsy revealed hemorrhage into ventricles

* Aggl. indicates agglutination method; congl., conglutination (albumin-plasma) method.

1. (*a*) Wiener, A. S., and Wexler, I. B.: Results of Therapy of Erythroblastosis with Exchange Transfusions, Blood **4**:1-35 (Jan.) 1949; Erythroblastosis Fetalis and Exchange Transfusion, in Litchfield and Dembo: Pediatric Progress, 1950. (*b*) Wiener, A. S.: Treatment of Erythroblastosis Fetalis by Exchange Transfusion, Postgrad. Med. **7**:1-10 (Jan.) 1950. (*c*) Bartel H., and von Loghem, I.: Treatment of 141 Infants Suffering from Hemolytic Disease of the Newborn by Exchange Transfusions, Riv. Ist. sieroterap. ital. (ser 2) **23**:268-278 (Oct.-Dec.) 1948. (*d*) Tzanck, A.; Bessis, M., and Buhot, S.: Clinical Studies of Therapy of Hemolytic Disease of Newborn With or Without Provoked Delivery by Means of Exsanguination Transfusion; Thirty-Four Cases, ibid. **23**:236-248 (Oct.-Dec.) 1948. (*e*) Raska, K.: The Treatment of Erythroblastosis Fetalis by Exchange Transfusion, ibid. **23**:249-263 (Oct.-Dec.) 1948. (*f*) Wallerstein, H.: Substitution Transfusion in Erythroblastosis Fetalis: Indications and Techniques, Proc. Am. A. Blood Banks, 1948, pp. 24-36. (*g*) Mollison, P. L., and Cutbush, M.: Exchange Transfusion in Haemolytic Disease of the Newborn, Lancet **2**:522-526 (Oct. 2) 1948. (*h*) Mustard, W. T., and Fraser, J.: Replacement Transfusion in Erythroblastosis Fetalis, Canad. M. A. J. **59**:378-379 (Oct.) 1948. (*i*) Allen, F. H., Jr.; Diamond, L. K., and Watrous, J. B.: Erythroblastosis Fetalis: V. The Value of Blood from Female Donors for Exchange Transfusion, New England J. Med. **241**:799-906 (Nov. 24) 1949.

type rh blood, bigravida and unipara, was sent to us at thirty-one weeks' gestation for a routine Rh-antibody titration. Her antibody titer proved to be 8 units by the agglutination method and 12 units by the plasma conglutination method. Four weeks later her titer was 24 units by both methods, and it was decided that the pregnancy should be interrupted. Accordingly, a cesarean section was performed five weeks before term, and a 5½ pound (2,500 Gm.) baby girl was delivered. A blood count taken one hour after birth revealed 2,900,000 red blood cells with a hemoglobin concentration of 11 Gm. (76 per cent); the stained smear showed 16 normoblasts per hundred white blood cells. Macrocytes and polychromasia were present. An immediate exchange transfusion was done, 550 cc. of group A, type rh blood being given and 490 cc. being withdrawn. In this case, as in all the others, the saphenous vein–

TABLE 5.—*Crude Mortality Rate Following Exchange Transfusion in Erythroblastosis Due to Rh Sensitization*

Investigator	Number of Cases	Deaths	Per Cent Mortality
Present study	34	4	10.7
Wiener and Wexler [14,15]	82	13	15.9
Bertel and von Loghem [16]	141	21	18.5
Tranek, Bessis and Buhot [16]	34	12	35.3
Rasks [16]	22	4	18.2
Wallerstein [17]	41	8	19.5
Mollison and Cutbush [18]	30	7	23.3
Mustard and Fraser [19]	24	3	12.5
Allen, Diamond and Watrous [21]	205	31	15.1

radial artery–heparin method used by Wiener and Wexler was employed. Five cubic centimeters of 10 per cent calcium gluconate was given at the middle and end of the transfusion to prevent hypocalcemia. (In later cases 1 cc. of calcium gluconate was given after every hundred cubic centimeters of blood transfused). The next day the red blood cell count was 5,600,000 and the hemoglobin concentration 13.5 Gm. (94 per cent). Three weeks later the hemoglobin concentration had fallen to 7.2 Gm. (50 per cent), and the red blood cell count was only 2,400,000. A transfusion of 80 cc. of group A, type rh blood was given at this time. For the next four weeks the reading of the hemoglobin content continued to drop, but it then began to rise and became normal when the baby was 3 months old. This case illustrates the timeliness of interrupting the pregnancy, as shown by the blood findings at birth. It is quite possible that this baby might have been stillborn, had the pregnancy been allowed to go to term.

Case 13 suggests the superiority of the exchange transfusion over multiple small transfusions. The mother, a group O, type rh multigravida, quadripara, had two normal children, but the third was erythro-

blastotic and was treated with several small transfusions. The child lived to be 9 months old, when it died from pneumonia. The baby did not develop normally, and from the description given by the mother, it is evident that the child manifested the neurologic sequelae of erythroblastosis. The fourth baby (the patient reported here) also was erythroblastotic, but he was treated by an exchange transfusion and has been normal to date (17 months old).

Case 23 is interesting in several respects. In the first place, the mother was a primipara, and no history of blood or plasma transfusion or the injection of any blood could be obtained. Apparently, then, erythroblastosis occurred in her first baby without any injection of blood to sensitize her, which is rather unusual, this being the second such family encountered in eighteen years of experience with erythroblastosis. Secondly, the baby manifested jaundice immediately after birth, which persisted for about seven weeks, in spite of a prompt exchange transfusion. Discussion of this aspect of the case will be presented later. When I first saw the baby, four hours after birth, he had a definite jaundice and pallor. The blood examination at this time revealed the following values: red cells, 2,900,000; white cells, 28,400, and hemoglobin content, 11.5 Gm. (80 per cent). The smear showed macrocytosis, polychromasia and 76 normoblasts per hundred white blood cells. The baby's cells were coated, and the reaction of the baby's cells with a strong anti-Rh_0 serum was very weak but was clearcut with anti-rh″ serum (the father's blood is type Rh_2). The mother's serum showed 48 units of Rh antibody by the albumin-plasma method and 4 units by the blocking technic. She belonged to group O, type rh.

An exchange transfusion was made six hours after the baby was born; 530 cc. of group O, type rh blood was given and 470 cc. withdrawn. A larger exchange transfusion had been contemplated, but, since the baby did not look well after this amount was given, it was deemed wiser to terminate the transfusion at this point. The baby acted better the next day, but the jaundice had deepened considerably. A blood examination revealed the following values: red cells, 5,200,000; hemoglobin content, 18 Gm. (122 per cent), and 126 normoblasts per hundred white blood cells. The next day the normoblasts had dropped to 53 per hundred white cells and three days later to 9 per hundred white cells. The deep jaundice persisted, and when the baby was 7 days old clay-colored stools were passed. At this time the icterus index was 47 units. In addition, there was tympanites, which responded to clyses of 5 per cent dextrose in saline solution. The jaundice, perhaps less pronounced, and clay-colored stools were still present on the seventeenth day, when the serum bilirubin was 21 mg. per hundred cubic centimeters, the alkaline phosphatase 8.2 units and the results of the cephalin flocculation and thymol turbidity tests negative. At this time the red blood cell

count had dropped to 2,460,000 and the hemoglobin content to 8 Gm. Two transfusions, of 60 cc. and 90 cc., respectively, were now given. On the fiftieth day the serum bilirubin had dropped to 6.4 mg. per hundred cubic centimeters, and the baby was discharged from the hospital four days later, the scleras still slightly icteric.

This case is evidence that hepatic damage can complicate erythroblastosis fetalis in spite of an immediate exchange transfusion. Perhaps a larger exchange transfusion would have prevented hepatic damage, but such a transfusion was not warranted because of the baby's condition. It is too early to say whether any permanent hepatic damage will result, but there seems to be little doubt that the prompt exchange transfusion played a significant role in saving this baby's life.

The mother of the baby in case 24 had had two previous erythroblastotic babies. In 1942, I was asked to see the first baby when she was 10 days old because she was very pale and jaundiced. At this time the red blood cell count was 1,400,000 and the hemoglobin content was 6.6 Gm. (46 per cent). The liver was 5 cm. and the spleen 2.5 cm. below the costal margin. Since the mother and baby both belonged to group A, 100 cc. of the mother's blood was given without delay, the role of Rh sensitization in erythroblastosis being little known in 1942. After this transfusion the red cells increased to 2,900,000 and the hemoglobin content rose to 10 Gm. (70 per cent). Another 100 cc. of the mother's blood was given five days later, and the next day the red cell count was 3,900,000 and the hemoglobin content 12 Gm. The third, and final, transfusion of 135 cc. of citrated blood was given a month later, when the red cell count was 2,200,000 and the hemoglobin content was 7.4 Gm. (52 per cent). The child is perfectly normal today.

In 1945, I was asked to treat this mother's second erythroblastotic baby. Within thirty-six hours this baby manifested jaundice and anemia. The blood examination showed the following values: red blood cells, 2,500,000; hemoglobin content, 11.5 Gm. (80 per cent); white blood cells, 40,000 and the smear revealed polychromasia, marked macrocytosis and 90 normoblasts per hundred white blood cells. A transfusion of 150 cc. of citrated group O, type rh blood was given at once. Six days later another 150 cc. of group O, type rh blood was given, and by now the jaundice had practically disappeared. Two weeks later the third and final transfusion of 150 cc. of blood was given. The baby did very well after that and is a normal child today.

The third erythroblastotic baby (case 24) was seen recently. This baby looked perfectly normal at birth, but within eighteen hours mild jaundice and anemia had developed. The blood examination showed the following values: red cells, 4,600,000; hemoglobin content, 15 Gm. (104 per cent), and white cells, 26,400; the smear revealed polychromasia, macrocytosis, and 36 normoblasts per hundred white blood cells. The

baby's cells were completely coated and "blocked," so that they typed as rh' instead of Rh_1 as would be expected from the father's type (Rh_1Rh_1). By the albumin-plasma conglutination method, the mother's serum showed 48 units of Rh antibody and 3 units by the blocking test.

The baby was given an exchange transfusion of 610 cc. of group O, type rh blood, 550 cc. of blood being withdrawn. Although the jaundice deepened considerably the next day, it began to recede in forty-eight hours, and in six days it was hardly visible. The baby left the hospital with his mother and is doing well, requiring no further transfusions. In view of the findings in this case, it seems to me that this baby might not have fared as well as his siblings if repeated small transfusions had been given, or, at least, recovery might not have been so prompt.

Cases 3 and 9 illustrate the bad prognosis one must give in the case of a mother who has previously lost a baby with erythroblastosis. We lost both of our babies from such families, which is not surprising, considering that in a series of 17 such cases Wiener and Wexler report a mortality of 41.2 per cent.

An exchange transfusion was done on a baby 3 days old for severe jaundice which later proved to be due to an obstruction of the duodenum. This baby appeared very sick, and, since the mother's blood was Rh negative, it was assumed that the baby was erythroblastotic, and an exchange transfusion was done without delay. At the end of the transfusion there was a marked drop in the icterus index. During the transfusion it was noticed that the baby was vomiting bile, and when on the following day the baby continued to vomit a surgeon was called into consultation. At his suggestion roentgenograms were taken, and a diagnosis of duodenal obstruction was made. The baby was operated on two days after the transfusion had been performed and made an uneventful recovery. He will be 3 years old in July and is perfectly normal. There seems hardly any doubt that the improvement in his general condition following the exchange transfusion made him a better subject for surgery and in this way contributed to saving a life.

An exchange transfusion was also done on a baby with congenital hemolytic icterus, because of early severe jaundice. In this baby also the jaundice subsided within a few days after the transfusion, and he did not require any further treatment for eight weeks. When jaundice appeared, two hours after birth, it was already known that the mother's blood was Rh negative but that her serum showed no Rh antibodies. It was also known that the father had had a splenectomy for congenital hemolytic icterus several years previously, making the diagnosis of this disease for the child highly probable. With this knowledge at hand, it was decided that an exchange transfusion could do no harm but would probably be beneficial, at least temporarily. From the subsequent favorable

course, it may be concluded that the exchange transfusion was helpful, and for that reason this case is reported. In this connection recent reports on the use of exchange transfusion in Cooley's anemia [2] are of interest.

COMMENT

As to the technic of exchange transfusion, as has already been mentioned, we have used the radial artery–saphenous vein technic of Wiener and Wexler. While most workers seem to feel that the umbilical catheter method of Diamond is simpler, I feel that the radial artery–saphenous vein technic has many advantages. First of all, the procedure is entirely open and the vessels used are expendable, whereas this is not true of the blind umbilical catheter method. Moreover, there have been deaths from embolism [3c] and thrombosis with the umbilical catheter method, and there is a greater danger of sepsis. Since blood is injected and withdrawn through the same catheter, there is a possibility of withdrawing blood which has just been introduced before the blood has mixed thoroughly with the baby's own blood. In fact, Raska [10] has reported 1 case in which he performed a 750 cc. exchange transfusion through the umbilical catheter, yet the differential agglutination test showed a replacement of 70 per cent instead of the calculated 95 per cent. This baby died at the age of 3 months of kernicterus. Finally, while neither Wiener and Wexler nor we have ever experienced a technical failure, such failures have occurred with the umbilical catheter technic, even in the hands of experts. Thus in a recent report of Diamond and others [11] at least five of the transfusions had to be terminated when less than 150 cc. of blood had been exchanged. In addition, the umbilical catheter technic cannot be safely applied after the umbilical vessels are thrombosed, and difficulties with the technic have led workers to devise modifications entailing cutting down on the umbilical vein after it enters the abdominal wall or cutting down on the greater saphenous vein in the inguinal region.

The assertion [3] that the large amount of citrate used in the procedure causes necrosis of the liver does not stand critical examination.[4] Thus, the results obtained by Wiener and Wexler were improved or, at least, were no worse when double the quantity of blood was used. The only danger is that of hypocalcemia, but this is easily averted by giving 1 cc.

2. (*a*) Folena, S.: Su alcuni cosi di morbo di cooley, Minerva pediat. **1**:196-198 (May) 1949. (*b*) Sansone: Su di un caso di malattia di cooley splenectomizatto e successivamenti trottato con exsanguinotransfusione, ibid. **1**:175-178 (May) 1949.

3. Rosenblatt, P.: Massive Necrosis of Liver Following Exchange Transfusion for Erythroblastosis Fetalis, Am. J. Clin. Path. **18**:700-715 (Sept.) 1948.

4. Wexler, I. B.; Pincus, J. B., Natelson, S., and Lugovoy, J. K.: The Fate of Citrate in Erythroblastotic Infants Treated with Exchange Transfusions, J. Clin. Investigation **28**:474-481 (May) 1949.

of 10 per cent calcium gluconate solution for every hundred cubic centimeters of blood injected. Since introducing this modification, we have had little or no operative morbidity and there has been no operative mortality. An exchange transfusion of 500 cc. usually takes only forty-five to sixty minutes and rarely more than two hours, while recently we were informed of a case in which a 500 cc. exchange transfusion by the "simpler" umbilical catheter method lasted nine hours.

Recently Diamond and his co-workers [11] have reported that by using female donors the mortality following exchange transfusion is reduced practically to zero. In our experience a female donor was used for only 1 patient (case 3), who died on the third day of kernicterus. Before offering a final opinion on the superiority of female donors over male donors in exchange transfusions, conservatism dictates that confirmation be awaited from other workers in this field.

SUMMARY

I wish to emphasize the following points: 1. Routine antepartum testing for Rh antibodies should be done on all Rh-negative multiparas and primiparas who give a history of blood transfusion or intramuscular injection of blood, if their husbands are Rh positive. 2. The timely interruption of a pregnancy in a sensitized woman may save the baby's life if it is followed up with an immediate exchange transfusion. 3. Exchange transfusion is more efficacious than multiple small transfusions in treatment of erythroblastosis; the mortality rate is lower, and among treated babies who survived neurologic sequelae have not occurred in my experience. 4. Exchange transfusion is more efficacious and therefore less costly. 5. Exchange transfusion need not be confined to the treatment of erythroblastosis, as it may be efficacious in other conditions, such as have been cited in this paper.

POLIOMYELITIS OF THE NEWBORN

Pathologic Changes in Two Cases

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OUR INTEREST in this subject was aroused by the death of a month old infant from the bulbar form of poliomyelitis in 1948. Clinical manifestations appeared at 2½ weeks of life after contact with an uncle acutely ill with poliomyelitis. Since that time we have observed 2 infants who had acute poliomyelitis in the newborn period, that is, in the first two weeks of life. We felt that a brief report of our experience with these 2 cases would be timely, as medical teaching generally has held that this disease does not occur in the newborn period because of immunity transmitted to the infant by the mother.

A review of the literature on poliomyelitis in the newborn revealed reports of 10 cases. Of these cases, 4 were reported as instances of "intra-uterine poliomyelitis." The reports of 3 of these cases[1] were based on histories taken two, thirty-two and fifty years respectively after the birth of the patient. In the fourth case[1c] poliomyelitis acquired prenatally was considered the most likely possibility to account for paralysis of the upper and lower limbs of an infant, present since birth. Critical analysis of the evidence for intrauterine infection in each case left the claim highly suspect if not untenable.

Of the remaining reports, that of Severin[2] in 1939 was well documented with clinical and cerebrospinal fluid findings, typical necropsy findings and successful transfer of the infection to an animal.

From the Section on Pediatrics (Dr. Mills), Mayo Clinic.

1. (*a*) Batten, F. E.: Does Poliomyelitis Occur During Intra-Uterine Life? Brain **33**:149-159, 1910. (*b*) Potts, C. S.: Intra-Uterine Poliomyelitis: Report of Case in Which Recrudescence of Symptoms Occurred After 50 Years, Arch. Neurol. & Psychiat. **21**:288-298 (Feb.) 1929. (*c*) Fishbein, M.: A Bibliography of Infantile Paralysis 1789-1944, with Selected Abstracts and Annotations, Philadelphia, J. B. Lippincott Company, 1946.

2. Severin, G.: Case of Poliomyelitis in New-Born, Nord. med. (Hygiea) **1**:55-58 (Jan. 7) 1939.

The other reports [3] were based on clinical and laboratory findings. In all these cases the disease was assumed to have originated from infected contacts, though definite history of contact was not present in each instance.

It is notable that in no previously reported case have clinical symptoms of poliomyelitis appeared before the fifth day of life. In only 1 other case [3a] has the mother been acutely ill, prodromes appearing about eighteen hours before delivery, and in that instance the infant had an onset of the disease on the eleventh day of life after being exposed to the mother on the first day. While it is well known that the incidence of poliomyelitis in pregnant women is increased,[4] in no instance has the fetus shown evidence of the disease. Harmon and Hoyne [5] in 1943 seemingly expressed the consensus of medical men when they stated, "in utero infection of the fetus occurs with rarity if at all." Though the incubation period is not absolutely fixed, evidence offered by Casey [6] and Aycock and Luther [7] indicates that the minimal time for development of the clinical disease is five days after exposure. Support of this viewpoint is given by Johns [3c] who reported the case of an infant delivered in a home in which one sibling had been acutely ill of poliomyelitis for two days and another had an onset on the infant's second day of life. On the fifth day of life the baby had fever and listlessness, on the seventh day muscular twitching and on the eleventh day flaccid paralysis of the left leg.

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3. (*a*) Biermann, A. H., and Piszczek, E. A.: A Case of Poliomyelitis in a Newborn Infant, J. A. M. A. **124**:296-297 (Jan. 29) 1944. (*b*) Gunewardene, T. H.: Acute Poliomyelitis in an Infant 12 Days Old, with Extensive Paralysis and Recovery, Lancet **2**:847 (Dec. 21) 1918. (*c*) Johns, A. W.: Multiple Cases of Acute Poliomyelitis, M. Officer **80**:230-231 (Nov. 20) 1948. (*d*) Mouton, C. M.; Smillie, J. G., and Bower, A. G.: Report of 10 Cases of Poliomyelitis in Infants Under 6 Months of Age, J. Pediat. **36**:482-492 (April) 1950. (*e*) Batten.[1a]

4. Baker, M. E., and Baker, I. G.: Acute Poliomyelitis in Pregnancy. Minnesota Med. **30**:729-734 (July) 1947. Fox, M. J., and Waisman, H. A.: Further Observations on Poliomyelitis in Pregnancy, Am. J. M. Sc. **214**:148-152 (Aug.) 1947. Kleinberg, S., and Horwitz, Thomas: The Obstetric Experiences of Women Paralyzed by Acute Anterior Poliomyelitis, Surg., Gynec. & Obst. **72**:58-69 (Jan.) 1941. Weaver, H. M., and Steiner, G.: Acute Anterior Poliomyelitis During Pregnancy, Am. J. Obst. & Gynec. **47**:495-505 (April) 1944. Brahdy, M. B., and Lenarsky, M.: Acute Epidemic Poliomyelitis Complicating Pregnancy, J. A. M. A. **101**:195-198 (July 15) 1933.

5. Harmon, P. H., and Hoyne, A.: Poliomyelitis and Pregnancy with Special Reference to the Failure of Fetal Infection: Two Hitherto Unreported Cases in One of Which the Human Fetal Spinal Cord Was Examined for the Virus, J. A. M. A. **123**:185-187 (Sept. 25) 1943.

6. Casey, A. E.: The Incubation Period in Epidemic Poliomyelitis, J. A. M. A. **120**:805-807 (Nov. 14) 1942.

7. Aycock, W. L., and Luther, E. H.: The Incubation Period of Poliomyelitis, J. Prevent. Med. **3**:103-120 (March) 1929.

Appearance of poliomyelitis before the fifth day of life, then, would indicate either an incubation period shorter than the present established minimum of five days or infection prior to birth. Though the virus is usually limited to the digestive tract and nervous system, as demonstrated by Sabin,[8] it has been isolated from the blood by Melnick and co-workers.[9] This fact indicates the possibility that blood-disseminated infection could reach the fetus of an acutely ill mother via the placenta.

REPORT OF CASES

CASE 1.—A boy was born at 2:20 a. m. on Aug. 11, 1949, while his mother was in a respirator critically ill with poliomyelitis of four days' duration. Outlet forceps were used to facilitate an uncomplicated vertex delivery. The obstetrician described the baby as an active normal boy, moderately asphyxiated, who responded to tracheal catheterization and insufflation and was taken to the nursery breathing normally about eight minutes after delivery.

On arrival at the nursery, examination revealed a robust, lustily crying infant boy with frothy, saliva-like material bubbling from the mouth. The hands and feet were slightly cyanotic, but respiratory movements were good and breath sounds clear throughout both lungs. The extremities moved readily, and the reflexes were active and bilaterally equal. The neurologic examination gave negative results.

The cyanosis cleared up completely, and the baby's course was uneventful until August 14, when a rectal temperature of 101 F. developed. There was no evidence of infection, and fever remained the only abnormality until 12:30 a. m., August 16, when listlessness and cyanosis of the lips and nail beds were noted. Significant findings were absence of response of the right foot and leg to pain and minimal response of the left. Mucus collecting in the mouth and pharynx was aspirated; oxygen therapy was started, and oral feedings were stopped. A lumbar puncture was done, and xanthochromatic fluid was obtained. The protein content of this fluid was 300 mg. per hundred cubic centimeters; the lymphocytes numbered 97 per cubic millimeter and the segmented (polymorphonuclear) leukocytes numbered 11 per cubic millimeter; an occasional erythrocyte was seen, and the value for sugar was 60 mg. per hundred cubic centimeters.

Intracranial hemorrhage and high cord injury were considered as possible causes for the clinical picture. Medical neurologic consultants considered subdural hematoma as likely.

Subdural taps through the anterior fontanel were carried out on August 16. No fluid could be obtained, although some clear fluid did drain from puncture sites before collodion pledgets were applied.

The patient became rapidly worse, with extreme flaccidity, irregular respiration and progressive cyanosis, and death occurred on August 17, on the seventh day of life.

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8. Sabin, A. B.: Etiology of Poliomyelitis, J. A. M. A. **117**:267-269 (July 26) 1941.

9. Ward, R.; Horstmann, D. M., and Melnick, J. L.: The Isolation of Poliomyelitis Virus from Human Extra-Neural Sources: IV. Search for Virus in the Blood of Patients, J. Clin. Investigation. **25**:284-286 (March) 1946.

Postmortem Examination.—Necropsy performed on the unembalmed body four and one-half hours after death disclosed essentially normal conditions except in the lungs and the central nervous system. Careful study of the heart did not reveal myocarditis.

In the lungs there were regions of collapse interspersed between regions of congestion and edema. On microscopic examination foci of early pneumonitis were seen.

In the central nervous system the leptomeninges were normal macroscopically except for congestion of the pial vessels. The falx and tentorium were normal. The brain was 60 Gm. heavier than the normal weight of 440 Gm. The convolutions were widened slightly, with commensurate narrowing of the sulci. On coronal section of the cerebrum, the white matter was moist and glistening, whereas the gray matter appeared normal. The ventricles and their ependymal lining were normal. The midbrain, medulla and cerebellum were normal. There was slight bulging of the cut surface of the cord, and the gray matter was a salmon pink without evidence of hemorrhage.

Microscopic examination revealed the characteristic findings of acute polioencephalomyelitis, with involvement of the cord, medulla, pons, midbrain, roof nuclei and vermis of the cerebellum, thalami, hypothalamus and the cortex of both motor areas and the left insula.

In the gray matter of the anterior horns in the cervical and lumbar enlargements, degenerative changes were evidenced by nearly complete loss of the ganglion cells and the presence of a heavy inflammatory infiltrate (fig. 1 *a* and *b*). Active neuronophagia was not seen, but occasionally pink-staining hyalinized remnants of ganglion cells were noted. The ganglion cells of the lateral and posterior columns revealed foci of degeneration with nests of inflammatory cells replacing them. Many of the remaining ganglion cells showed degenerative changes characterized by peripheral clumping of the Nisal substance. Sections taken from the remaining levels of the cord revealed the loss of neurons as well as the inflammatory reaction to be more focal in distribution (fig. 1 *c*).

In the medulla, the motor nuclei of the cranial nerves and the inferior olivary nuclei revealed focal loss of ganglion cells with aggregates of inflammatory cells. In the lateral and medial reticular substance there was a scattered, diffuse inflammatory infiltrate.

In the midbrain, accumulations of inflammatory foci were marked and widespread. In some instances, these foci resembled microabscesses with a preponderance of neutrophils. In other instances, sites of softening were seen with the loss of brain substance, which was replaced by swollen, vacuolated cells that resembled neutrophils and microglia which appeared to be active in phagocytosis (figs. 1 *d* and 2 *a*).

The pons exhibited rather severe involvement of the nuclei in the floor of the fourth ventricle, and to a less extent the pontile nuclei were the site of focal damage. The hypothalamus was extensively involved, whereas the thalami exhibited scattered focal involvement. The roof nuclei of the cerebellum presented rather marked loss of ganglion cells and the characteristic cellular response. Involvement of the dentate nuclei was focal.

The reaction in the cortex was limited to both motor areas and the left insula (fig. 2 *b*). The cellular response tended to be limited to small foci which had replaced the ganglion cells in the midzone of the cortical cell layer.

Perivascular cuffs of lymphocytes admixed with a few neutrophils were seen throughout the cord and the brain. This was particularly pronounced in the midbrain and the hypothalamus (fig. 2 *c*). Active neuronophagia (fig. 2 *d*) by

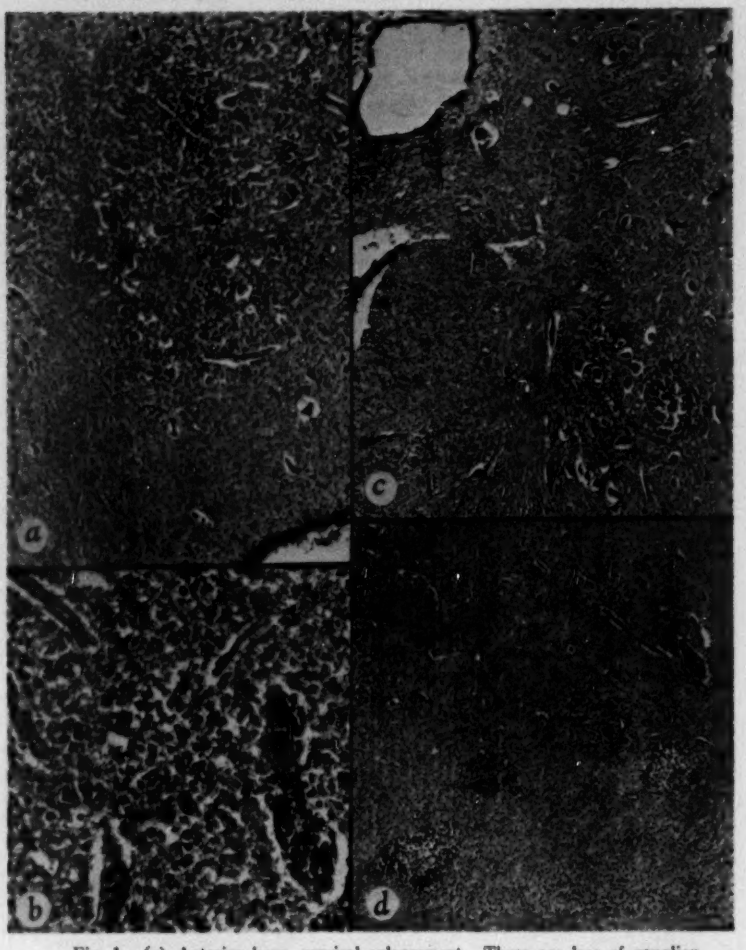

Fig. 1.—(*a*) Anterior horn, cervical enlargement. There are loss of ganglion cells, increased vascular markings and heavy inflammatory infiltrate. Hematoxylin and eosin; × 60. (*b*) Anterior horn, lumbar enlargement. There are lack of neutrophils, perivascular cuffing by inflammatory cells and phagocytosis. Hematoxylin and eosin; × 175. (*c*) Focal involvement of the anterior horn of the thoracic cord. Hematoxylin and eosin; × 60. (*d*) Midbrain. Foci of softening and a diffuse inflammatory infiltrate are shown. Hematoxylin and eosin; × 24.

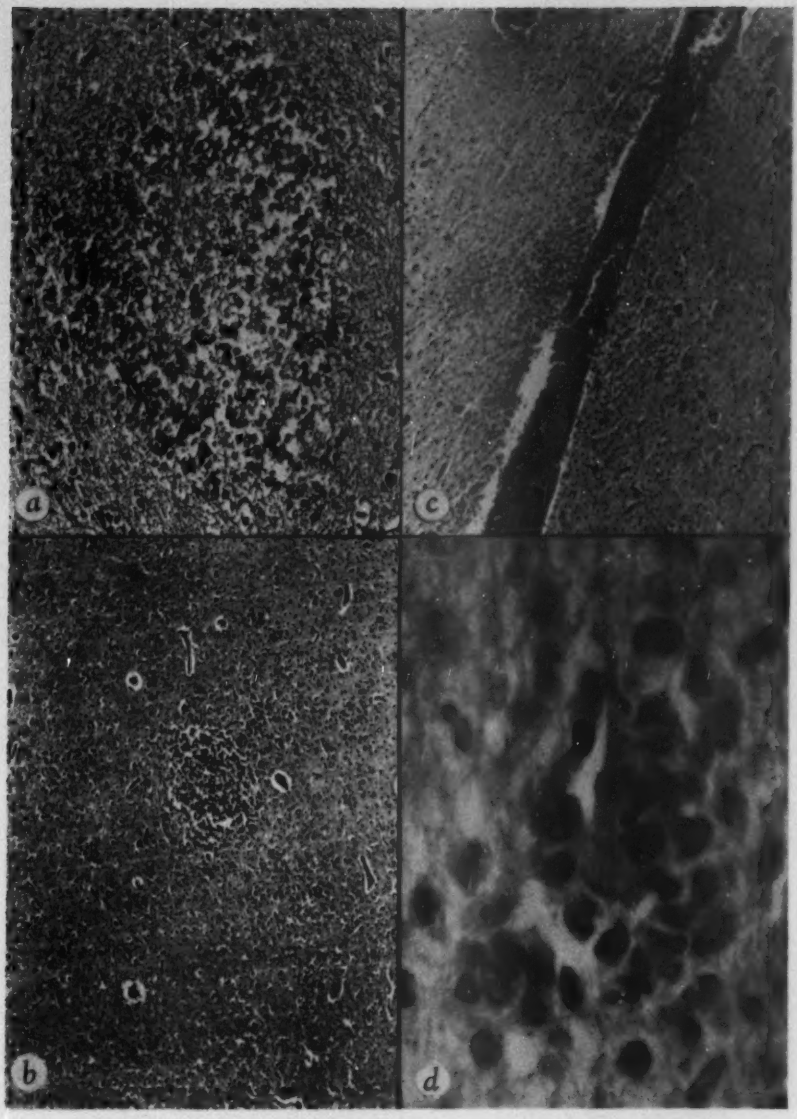

Fig. 2.—(*a*) Midbrain. This is an enlargement of the left lower corner of figure 1*d*. Active phagocytosis and necrosis of brain substance are evident. Hematoxylin and eosin; × 140. (*b*) Right motor cortex. This is one of the sites of cortical involvement. Hematoxylin and eosin; × 60. (*c*) Hypothalamus. Intense perivascular cuffing by lymphocytes, macrophages and a few neutrophils is shown. Hematoxylin and eosin; × 75. (*d*) Hypothalamus. This is one of the rare examples of neuronophagia by mononuclear cells and neutrophils. Hematoxylin and eosin; × 1,100.

histiocytes and neutrophils was rarely seen, and only the late stage of lysis of ganglion cells could occasionally be demonstrated. Nuclear inclusion bodies were not found. Numerous ganglion cells in the less involved parts were observed to have undergone central chromatolysis with peripheral clumping of the Nissl substance.

In general, the inflammatory infiltrate consisted of lymphocytes, neutrophils and mononuclear cells in about equal proportions. In several instances, foci were observed in which the nature of the infiltrate was more acute, suggesting that these foci represented a more recent destruction of ganglion cells or a higher concentration of the virus. Where the softening was more marked, the acute features of the reaction were subsiding and phagocytosis of the necrotic tissue was demonstrable (fig. 2*a*).

In the cervical enlargement, where destruction of the gray matter was pronounced, the astrocytes of the adjacent white matter were swollen and were more prominent than in a control series of comparable sections from infants of the same age group. It is of interest that the infiltration in the arachnoid was moderately pronounced and that the composite cells were in approximately the same ratio as they were in the last spinal fluid examined.

Sections from the placenta in this case were studied and no abnormality found. The placentas of 3 other women acutely ill with poliomyelitis were also found to be essentially normal.

Through the cooperation of Dr. Claus W. Jungeblut, Department of Bacteriology, Columbia University, New York, tissue in this case was inoculated into Cynomalgus monkeys, resulting in the development of lesions typical of poliomyelitis in the animals. A report of viral passage studies, of which this case was a part, will be made by Dr. Jungeblut and associates at a later date.

Comment on Case 1.—From the over-all microscopic picture, we can conclude that the virus had been active for a period of at least four days. The criteria for this conclusion have been based on four findings: 1. There was apparent regression of the neutrophils as evidenced by their phagocytic activity and their decreased numbers in such places as the cervical portion of the cord. 2. Neuronophagia, except in rare instances, had been completed, and the apparent recovery phase of many ganglion cells, as described by Bodian,[10] was manifested by the peripheral clumping of the Nissl substance. 3. The phagocytic activity of the mononuclear cells and the activity of the microglia were demonstrable. 4. The response of the astrocytes to the tissue destruction of the cervical enlargement was definite.[11]

CASE 2.—A normal boy was born Nov. 10, 1949, after uncomplicated labor and delivery. On November 12 his mother had the onset of acute poliomyelitis, but the baby showed no signs of illness. He continued to do well, but on November 15 examination of spinal fluid obtained by lumbar puncture disclosed a lymphocyte count of 5, a segmented (polymorphonuclear) leukocyte count of 1, a protein content of 40 mg. and sugar content of 45 mg.

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10. Bodian, D.: Histopathologic Basis of Clinical Findings in Poliomyelitis, Am. J. Med. **6**:563-578 (May) 1949.

11. Baggenstoss, A. H.; Kernohan, J. W.; and Drapiewski, J. F.: The Healing Process in Wounds of the Brain, Am. J. Clin. Path. **13**:333-348 (July) 1943.

There was no change until November 18, when a rectal temperature of 101 F. and listlessness were noted. The next day the extremities became flaccid, and respirations increased to 52 per minute. By November 21 flaccid quadriplegia, irregular, rapid, shallow respirations and inability to swallow had developed. Examination of the cerebrospinal fluid at that time revealed a lymphocyte count of 32, a segmented leukocyte count of 12, a protein content of 120 mg. and sugar content of 53 mg. The clinical course was rapidly downhill, with death on November 24.

Postmortem Examination.—At necropsy, performed on the unembalmed body three hours after death, the abnormal findings were restricted to the heart, lungs and the central nervous system.

In the heart no gross abnormality was noted. Histologic evidence of severe acute and healing myocarditis was found in sections taken from the ventricular septum, the left posterior papillary muscle and the lateral wall of the left ventricle. The findings closely paralleled those of Ludden and Edwards [12] in their study of carditis in poliomyelitis. Focal necrosis of muscle fibers and cellular infiltration of varying degrees were widespread, and the sites of these changes were interspersed frequently among sites of an older healing process. The foci of necrosis varied in size from that of three or four muscle fibers to that of a large number (fig. 3*a*).

In the sites of acute myocarditis, the muscle fibers were replaced by pink-staining, amorphous clumps of degenerating cytoplasm. Frequently the sarcoplasm had undergone a hyaline change, which Boucek and co-workers [13] thought to represent a later stage in the disease process (fig. 3*b*). There was a gradual transition from the normal tandem fibers to that of degeneration as evidenced by splitting of fibers, loss of cross striations and occasionally vacuolation of the cytoplasm. The nuclei of the muscle fibers appeared shrunken in the early stages and disappeared as the process advanced. The cellular infiltrate was moderately abundant, consisting chiefly of large mononuclear cells and to a less degree of lymphocytes and plasma cells (fig. 3*c*). In some instances there was a light scattering of neutrophils.

Interspersed among the foci of more acute degeneration were foci of healing which were characterized by myocardial stroma from which the necrotic muscle fibers had been removed. Many large mononuclear cells and a few lymphocytes and plasmacytes (plasma cells) were seen in the interstices of the stroma (fig. 4). Early fibroblastic proliferation was also seen.

In the interstitial connective tissue there was a moderate amount of edema, which was most marked about the small blood vessels. The capillaries were congested in some places, and occasional foci of extravasated erythrocytes were seen.

In the lungs, gross and microscopic examination disclosed patchy sites of collapse without evidence of pneumonitis. The capillaries were moderately congested.

In the central nervous system, the falx, tentorium and leptomeninges were normal. The weight of the brain was 430 Gm. (normal 440 Gm.), and its external appearance was not unusual. On coronal section the reticular substance in the

12. Ludden, T. E., and Edwards, J. E.: Carditis in Poliomyelitis: An Anatomic Study of 35 Cases and Review of the Literature, Am. J. Path. **25**:357-381 (May) 1949.

13. Boucek, R. J.; Bailey, A. A.; Burchell, H. B., and Edwards, J. E.: Cardiac Clinics: CXXX. Myocardial Disease in Acute Poliomyelitis, Proc. Staff Meet., Mayo Clin. **24**:495-500 (Sept. 14) 1949.

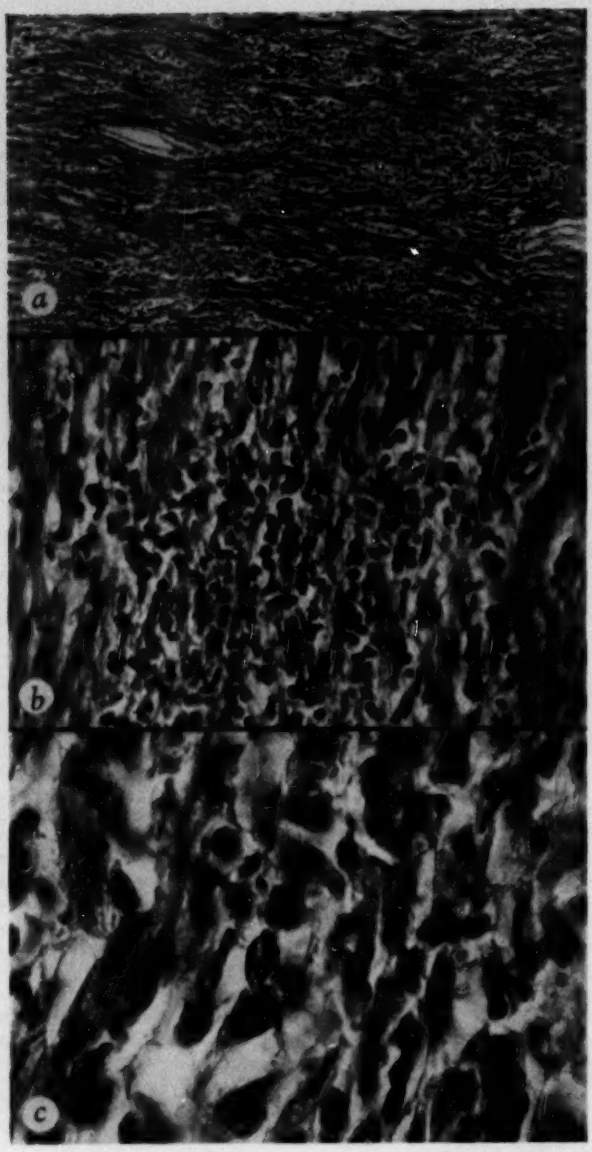

Fig. 3.—(*a*) Posterior papillary muscle of the left ventricle of the heart. Focal loss of muscle fibers and cellular infiltrate are shown. Hematoxylin and eosin; × 85. (*b*) Acute myocarditis with degenerating muscle fibers and cellular infiltrate consisting of macrophages, lymphocytes and plasma cells is disclosed. Hematoxylin and eosin; × 320. (*c*) Loss of striation and hyalinization of the sarcoplasm of muscle fibers are demonstrated. Striations are still discernible in the fiber on the left. Mallory's phosphotungstic acid hematoxylin stain; × 675.

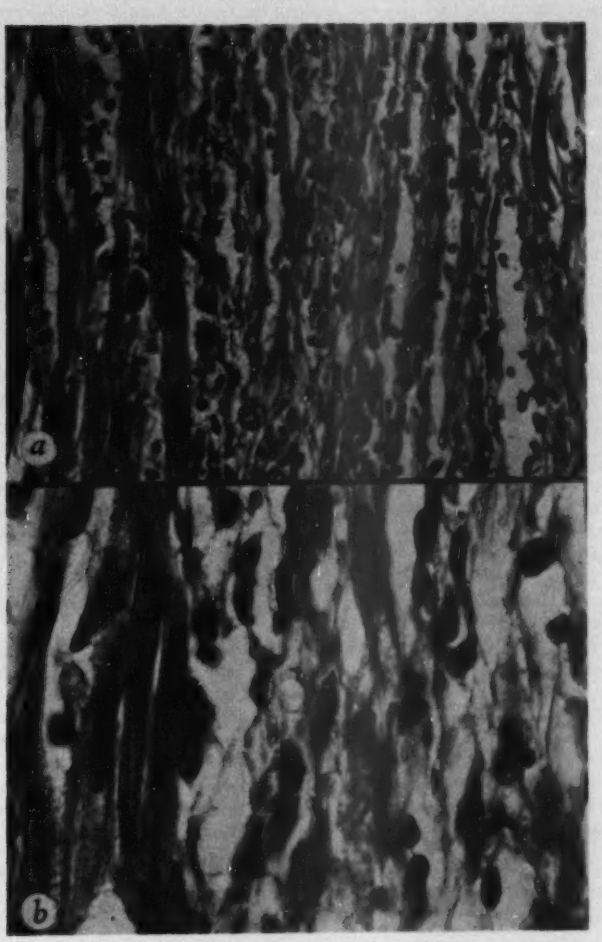

Fig. 4.—(*a*) Ventricular septum. Healing myocarditis with loss of muscle fibers, condensation of stroma and early proliferation of fibroblasts is shown. The cellular infiltrate consists of large mononuclear cells, lymphocytes and a few plasma cells. Hematoxylin and eosin stain; × 320. (*b*) Posterior papillary muscle of the left ventricle of the heart. Myocardial stroma with nearly complete removal of the degenerated sarcoplasm is seen. Mallory's phosphotungstic acid hematoxylin stain; × 675.

medulla was faintly pink and bulged slightly above the cut surface. A single hemorrhagic needle tract was seen entering the anterior horn of the left ventricle. The spinal cord was adjudged normal.

Microscopic examination revealed typical evidence of acute polioencephalomyelitis, with involvement of the cord, medulla, roof nuclei of the cerebellum and the thalami. The sections of the cervical and thoracic parts of the cord demonstrated the severest reaction. In the cervical enlargement the ganglion cells of the anterior columns were destroyed, while a few ganglion cells were still discernible in the posterior columns. These ganglion cells demonstrated marked peripheral clumping of the Nissl substance, with a perinuclear clear zone. Scattered, shrunken, granular, eosinophilic masses were seen in the more reactive zones, which represented ganglion cells that had undergone degeneration by lysis. No neuronophagia or inclusion bodies were demonstrated.

The inflammatory infiltration was moderately severe. The infiltrate consisted of numerous large mononuclear cells, which frequently displayed a vacuolated cytoplasm. There were also moderate numbers of lymphocytes and plasma cells admixed with a few neutrophils.

The capillaries were congested and in part surrounded by a cuff of mononuclear cells. The ground substance of the gray matter appeared somewhat soft, but the astrocytes were not unusually prominent.

In the thoracic segments of the cord the reaction was more pronounced in one anterior column and, in general, not so severe as in the cervical enlargement. Lysis of ganglion cells was apparent, with rare focal accumulations of inflammatory cells. A moderately marked inflammatory reaction was diffusely distributed throughout the anterior and lateral columns. Phagocytic activity by the mononuclear cells was rarely observed.

In the lumbar segments of the cord there was equal involvement of the two anterior columns in about the same intensity as that of the more severely involved thoracic region.

In the reticular substance of the medulla there was moderately severe, diffuse destruction of ganglion cells accompanied with light diffuse inflammatory infiltration. The nuclei of the cranial nerves were not conspicuously involved. The roof nuclei of the cerebellum and the thalami contained a few scattered foci of inflammatory cells. Perivascular cuffing by lymphocytes and mononuclear cells was for the most part confined to the sites of parenchymal involvement.

The results of viral passage studies, undertaken by Dr. Claus W. Jungeblut at the time of this writing, on tissues in this case will be reported at a later date in conjunction with a report of case 1.[14]

Comment on Case 2.—In this case the significantly involved parts of the central nervous system were confined to the cord and the medulla. The thoracic part of the cord demonstrated more complete involvement of one anterior column, which correlates with the clinical observation pertaining to the lack of function of the right intercostal muscles. The cervical portion of the cord was the only part in which there was softening of the ground substance and phagocytosis. One gains the impression that many of the ganglion cells in the lower segments of

14. Successful transfer of the virus from tissues of the patient in case 2 to Cynomalgus monkeys has just been reported to us by Dr. Jungeblut.

the cord would have regained their function had the reticular substance of the medulla and the cervical part of the cord maintained a minimal number of functioning neurons.

No conclusions can be drawn from the clinical history as to cardiac function. In view of the fact that moderately severe bulbar poliomyelitis was demonstrated, one can do little more than speculate as to the contributory effect of the myocarditis in the death of this patient. However, the severity and the wide distribution of the myocarditis leave one with the impression that it contributed in no small degree to the fatal termination.

SUMMARY AND CONCLUSIONS

A brief review of poliomyelitis in the newborn and a report of 2 cases are presented. A review of the literature revealed no previous case in which prodromes in the infant appeared as early as three and one-half days of life. In no reported case had the mother had acute febrile poliomyelitis of four days' duration at the time of birth. In one report the mother had had prodromes the day before delivery, but in that instance the infant did not become ill until the eleventh day of life, after exposure to its mother for ten minutes on the first day of life. In view of the fairly well established fact that the minimal incubation period of clinical poliomyelitis is five days and that immediate isolation of the infant in the first case was carried out on delivery, his illness appeared either after an incubation of only three and one-half days or resulted from an intrauterine infection. On the basis of this evidence it is no longer possible to assume that newborn infants are immune to poliomyelitis.

ELECTROCARDIOGRAPHIC OBSERVATIONS IN POLIOMYELITIS

Changes of the Q-T Interval in Twenty-Three Cases

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RANTZ [1] has recently reviewed the problem of myocarditis occurring in infections of all types: bacterial, rickettsial, virus and parasitic. Other authors [2] have reported clinical, electrocardiographic and anatomic observations suggesting myocardial dysfunction in a wide variety of infectious illness. Gore,[3] in reviewing a large amount of pathologic material, noted a striking incidence of myocardial disease among patients who died from infectious disease. Electrocardiographic studies in this type of illness have not been frequent or extensive.

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1. Rantz, L. A.: Myocarditis in Infections, with a Selected Bibliography, Stanford M. Bull. **7**:12, 1949.

2. Master, A. M.; Romanoff, A., and Jaffe, H.: Electrocardiographic Changes in Pneumonia, Am. Heart J. **6**:696, 1931. Thomson, K. J.; Rutstein, D. D.; Tolmach, D. M., and Walker, W. H.: Electrocardiographic Studies During and After Pneumococcus Pneumonia, ibid. **31**:565, 1946. Settle, E. B.; Pinkerton, H., and Corbett, A. J.: A Pathologic Study of Tsutsugamushi Disease (Scrub Typhus) with Notes on Clinico-Pathologic Correlation, J. Lab. & Clin. Med. **30**:639, 1945. Rosenberg, D. H.: Acute Myocarditis in Mumps (Epidemic Parotitis), Arch. Int. Med. **76**:257 (Nov.-Dec.) 1945. Wendkos, M. L., and Noll, J., Jr.: Myocarditis Caused by Epidemic Parotitis, Am. Heart J. **27**:414, 1944. Bang, O.: Gonorrheal Myocarditis, Brit. M. J. **1**:117, 1940. Finland, M.; Parker, F., Jr.; Barnes, M. W., and Joliffe, L. S.: Acute Myocarditis in Influenza A Infections, Am. J. M. Sc. **209**:455, 1945. Degen, J. A.: Visceral Pathology in Measles: A Clinico-Pathologic Study of 100 Fatal Cases, ibid. **194**:104, 1937. Lillie, R. D.: Pathology of the Eastern Type of Rocky Mountain Spotted Fever, Pub. Health Rep. **46**:2840, 1931. Brick, M.: Ueber Herzveränderungen bei Pertussis, Virchows Arch. f. path. Anat. **212**:404, 1913. Kirch, E.: Pathologie des Herzens, Ergebn. d. allg. Path. u. path. Anat. (Abt. I) **22**:1, 1927. Herzog, E., and Rodriguez, H.: Die Beteiligung des Myocards beim Fleckfieber (Myocarditis exanthematica), Beitr. z. path. Anat. u. z. allg. Path. **96**:431, 1936.

3. Gore, I.: Myocarditis in Infectious Diseases, Am. Pract. **1**:292, 1947.

Saphir [4] has recently reviewed current concepts of myocarditis associated with virus diseases. Viruses have been recovered from patients who have died from myocarditis, and electrocardiographic changes have been observed in patients with well recognized virus disease. In some cases, myocarditis may be detected clinically and not infrequently may be the cause of death. Virus myocarditis, pathologically simulating that in man, has been produced in various experimental animals.[5]

Myocarditis in man has been reported in association with various virus diseases, which include infectious hepatitis, yellow fever, varicella, dengue, primary atypical pneumonia, rubeola, mumps, poliomyelitis, influenza-like infections and others.[4] Myocardial involvement during the course of such illnesses may often be overlooked. The frequent occurrence of circulatory failure during and after the influenza pandemic of 1918 is of possible interest in this regard.

Saphir and Wile [6] first reported myocarditis as a complication of poliomyelitis in 1942. Six of seven hearts from patients who died during or after poliomyelitis showed histologic evidence of myocarditis. Peale and Lucchesi [7] reported 7 fatal cases of bulbospinal poliomyelitis in 1943. In 1 case moderately severe myocarditis was demonstrated histologically; in 4 there were minimal changes, while 2 revealed no changes. In the same year Dublin and Larson [8] reported 2 cases of myocarditis among 12 fatal cases of acute poliomyelitis. Saphir [9] in 1945 described myocarditis in 10 of 17 patients with poliomyelitis autopsied.

Ludden and Edwards [10] recently reported histologic evidence of myocarditis in 14 of 35 cases of poliomyelitis studied. Boucek and associates,[11] observed nonspecific electrocardiographic abnormalities in

4. Saphir, O.: Virus Myocarditis, Mod. Concepts Cardiovas. Dis. **18**:43, 1949.

5. Helwig, F. C., and Schmidt, E. C. H.: A Filter-Passing Agent Producing Interstitial Myocarditis in Anthropoid Apes and Small Animals, Science **102**:31, 1945. Schmidt, E. C. H.: Virus Myocarditis: Pathologic and Experimental Studies, Am. J. Path. **24**:97, 1948. Warren, J., and Smadel, J. E.: Further Observations on the Virus of Encephalomyocarditis, abstracted, J. Bact. **51**:615, 1946. Saphir.[4]

6. Saphir, O., and Wile, S. A.: Myocarditis in Poliomyelitis, Am. J. M. Sc. **203**:781, 1942.

7. Peale, A. R., and Lucchesi, P. F.: Cardiac Muscle in Poliomyelitis, Am. J. Dis. Child. **65**:733 (May) 1943.

8. Dublin, W. B., and Larson, C. P.: Pathologic Findings in Poliomyelitis, Am. J. Clin. Path. **13**:15, 1943.

9. Saphir, O.: Visceral Lesions in Poliomyelitis, Am. J. Path. **21**:99, 1945.

10. Ludden, T. E., and Edwards, J. E.: Carditis in Poliomyelitis: An Anatomic Study of 35 Cases and a Review of the Literature, Am. J. Path. **25**:337, 1949.

11. Boucek, R. J.; Bailey, A. A.; Burchell, H. B., and Edwards, J. E.: Cardiac Clinics: CXXX. Myocardial Disease in Acute Poliomyelitis, Proc. Staff Meet., Mayo Clin. **24**:495, 1949.

a fatal case of bulbospinal poliomyelitis. At autopsy the heart showed edema throughout the myocardium, minor cellular infiltration in some areas and severe necrotizing degenerative focal lesions.

Gefter and associates [12] have reviewed electrocardiograms made from 226 patients with poliomyelitis. Abnormalities were found in 32 (14.2 per cent). There was little change in the frequency of electrocardiographic abnormalities as the duration of the disease increased, suggesting that such changes occur early and tend to persist several weeks. The incidence of the abnormal findings in the 226 patients was as follows: Tachycardia disproportionate to fever, 9 patients (4.0 per cent); extrasystoles, 2 patients (0.9 per cent); abnormally high and peaked P waves, 6 patients (2.7 per cent); prolonged P-R interval, 7 patients (3.1 per cent); abnormal slurring of the QRS complex, 1 patient (0.4 per cent); left axis deviation, 8 patients (3.5 per cent); right axis deviation in addition to other abnormalities, 5 patients (2.2 per cent); abnormal deviation of the RS-T segment, 5 patients (2.2 per cent), and flat, diphasic or inverted T waves, 8 patients (3.5 per cent). Since no fatal cases were included in this series, pathologic correlation with these findings was not possible. Clinical evidence was generally insufficient to support a diagnosis of carditis. These authors pointed out, however, that myocarditis may exist in association with certain acute infectious diseases, even though clinical findings are minimal or absent.[13] Neubauer's electrocardiographic observations in other infectious diseases [13a] did not differ greatly from those of Gefter's group,[12] who reported only poliomyelitis.

Measurement of the Q-T interval, corrected for rate,[14] has recently been proposed as a diagnostic aid in the detection of active rheumatic carditis.[15] Prolongation of the corrected Q-T interval (Q-Tc) in active carditis is said to indicate disturbed myocardial efficiency, since the systole (Q-T) of the diseased myocardium is prolonged at the expense of the diastolic resting phase (T-Q) of the cardiac cycle. Theoretically,

12. Gefter, W. I.; Leaman, W. G., Jr.; Lucchesi, P. F.; Mager, I. E., and Dworin, M.: The Heart in Acute Anterior Poliomyelitis, Am. Heart J. **33**:228, 1947.

13. (*a*) Neubauer, C.: Myocarditis in Acute Infective Diseases: Review of 200 Cases, Arch. Dis. Childhood **19**:178, 1944. (*b*) Gefter and others.[12]

14. Bazett's formula (Bazett, H. C.: An Analysis of the Time-Relations of Electrocardiograms, Heart **7**:353, 1918-1920) corrects the measured Q-T interval for heart rate as follows: $Q\text{-}Tc = \frac{Q\text{-}T \text{ (seconds)}}{\sqrt{\text{Cycle length (seconds)}}}$.

15. (*a*) Taran, L. M., and Szilagyi, N.: The Duration of the Electrical Systole (QT) in Acute Rheumatic Carditis in Children, Am. Heart J. **33**:14, 1947. (*b*) Abrahams, D. G.: The Q-T Interval in Acute Rheumatic Carditis, Brit. Heart J. **11**:342, 1949.

one would expect prolongation of the Q-Tc interval in the presence of myocarditis, whatever its origin.

Electrocardiographic studies of myocarditis in other infectious diseases or in acute poliomyelitis have not included a discussion of the possible diagnostic significance of the Q-Tc interval. It is the purpose of the present report to evaluate the cardiac status of patients during and following acute poliomyelitis and especially to point out the changes in the Q-T interval in the electrocardiogram as a possible diagnostic aid. Clinical and electrocardiographic observations were recorded on 23 children with poliomyelitis and parallel observations on 55 control patients.

METHOD

Electrocardiograms were made with a direct-writing machine. Each tracing consisted of three standard limb leads, three augmented unipolar limb leads (aVL, aVR and aVF) and six unipolar chest leads (V_1, V_2, V_3, V_4, V_5 and V_6). Altogether 23 patients with acute poliomyelitis were studied during the late summer and early fall of 1949. Tracings were obtained shortly after admission of the patient to the hospital. At least one follow-up tracing was made within two to four days for each patient whose initial electrocardiogram was read as normal. When abnormalities were discovered, a series of tracings was made at similar intervals until the return of the electrocardiographic change to normal or until the discharge of the patient. One patient was observed on whom follow-up observations were not made. Each patient was examined for clinical evidence of cardiovascular disease. The clinical course, extent and severity of paralysis, duration of illness, duration of fever and height of abnormal temperature were recorded in each case. The diagnosis of acute anterior poliomyelitis was made according to clinical criteria, with the aid of standard laboratory procedures, including routine examination of the spinal fluid.

Parallel clinical and electrocardiographic observations were made during the same period on 55 control patients without evidence of cardiovascular disease. These patients were selected at random from pediatric hospital admissions and from a diagnostic clinic for rheumatic fever. Only children with no clinical or laboratory evidence of disease were considered acceptable from the latter source. Patients with a past or present history of rheumatic fever were excluded. Eighty-two control electrocardiograms were made. Thirty-three patients in the control series had only a single electrocardiogram.

The Q-T interval and the corresponding cycle length (R-R) were measured with the aid of a hand magnifying lens in the shortest and longest cycle in each of six leads: three limb leads and three chest leads, including at least two left precordial leads. The average of these intervals was then obtained, and correction of the Q-T interval was made for heart rate with use of Bazett's formula. This procedure, according to Taran,[16] minimizes the effects of respiratory variations such as sinus arrhythmia and yields a measurement (Q-Tc) which includes a suitable variety of electrocardiographic projections.

The upper limit of normal for the Q-Tc interval has been stated as 0.405 second for children [15a] when tracings are made under conditions simulating basal conditions. This value may be somewhat greater for adults: 0.415 second for men and 0.420

16. Taran, L. M.: Personal communication to one of the authors (H. A. J.).

second for women. Since basal conditions are difficult to achieve in children in the circumstances in which electrocardiograms must often be made, we have accepted a 5 per cent increment as a doubtful range. The significance of doubtful values may be affected by subsequent clinical and electrocardiographic events. Such findings must be carefully followed and evaluated in the light of the total clinical picture.

RESULTS

Abnormalities of Rhythm, Rate and Conduction.—Sinus tachycardia of a marked degree, that is, in excess of that expected from the fever and toxicity of the patient, was noted in 4 patients (J. C., R. D., B. P. and S. R.). R. D. had a prolonged Q-Tc interval, and the Q-Tc interval of S. R. was equivocal. Arrhythmias other than first degree heart block were not encountered. The P-R interval was prolonged for age and rate [17] in 1 patient (G. L.). The P-R interval lengthened after four normal measurements after admission and returned to the normal range after one week. A prolonged Q-Tc interval was also observed in this patient. One other patient (S. R.) showed slight prolongation of the P-R interval, which was transient and was associated with an equivocal Q-Tc interval.

P Waves and QRS Complex.—No abnormalities of P waves were encountered in the present series. Two patients (R. G. and D. P.) showed a tendency toward right axis deviation. In 1 patient (D. P.) this was associated with a prolongation of the Q-Tc interval. Definite right axis deviation was seen in 3 patients (R. H., E. H. and F. S.). E. H. also had a prolonged Q-Tc interval. F. S. had, in addition, a prominent R wave in lead V_1 and a marked tachycardia. His Q-Tc interval was within normal limits. No left axis deviation was encountered in the series.

The R wave was prominent and notched in leads V_1 and V_2 in 1 patient (B. A.). Notching of the R wave in lead V_1 was observed in another patient (S. R.).

S-T Junction and S-T Segment.—No definitely significant deviation of the S-T junction or of the S-T segment was observed in this series.

T Waves.—Definitely abnormal T waves were encountered in 1 patient (J. C.). The changes were transient, however, and were associated with fever and marked tachycardia in a severely, acutely ill patient. The case will be reviewed briefly.

Case 1.—J. C., a 6 year old Negro girl, was admitted to the hospital Oct. 22, 1949, complaining of headache and stiff neck of three days' duration. Her temperature had been elevated during the preceding twenty-four hours, during which period she had vomited and complained of pain in her abdomen and legs. No muscle weakness could be demonstrated, although both neck and spine were rigid. Her

17. Ashman, R., and Hull, E.: Essentials of Electrocardiography for the Student and Practitioner of Medicine, New York, The Macmillan Company, 1937.

temperature was 39.5 C. (102.3 F.) and pulse rate 150 per minute. There was a systolic murmur of grade 4 intensity, loudest at the base of the heart and transmitted chiefly to the neck and back. The heart was not enlarged to percussion or on roentgenograms. Cultures of the spinal fluid were sterile. An electrocardiogram made shortly after admission showed a verticle heart with the inversion of T waves in all leads except aVR, in which the T wave was upright. The patient was placed in oxygen intermittently during the forty-eight hours following admission and then removed from oxygen entirely. She seemed much improved after this time, and an electrocardiogram on October 24 showed that the T waves had become upright in all limb leads, aVF, and V_4, V_5 and V_6 and inverted in lead aVR. Subsequent tracings were entirely normal. The Q-Tc interval was never prolonged. As the patient improved, the basal murmur noted on admission became much less pronounced and was weakly transmitted.

Such transient changes of the T waves are probably insufficient evidence to support a diagnosis of myocarditis. This is a nonspecific finding which could be caused by a temporary relative myocardial hypoxia as a result of the marked tachycardia. Mechanically induced fever,[18] or fever resulting from the intravenous injection of typhoid vaccine [19] may cause transient electrocardiographic changes, the physiologic significance of which is not understood.

Q-Tc Interval—The Q-Tc interval was considered definitely prolonged in 5 patients, equivocal in 3, and normal in 15 (table). Among the 5 patients in whom the Q-Tc was prolonged, it returned to normal in 1 patient (G. L.) within a period of thirty days. In the second patient (E. H.) the Q-Tc interval rose to 0.451 second and then declined during the following two weeks, after which time the patient was lost from observation. In 2 patients the Q-Tc interval remained the same (D. P.) or varied from week to week at prolonged levels (R. D.). The fifth patient (A. C.), without paralysis (Q-Tc interval 0.437 second), was discharged before follow-up tracings could be obtained. In no patient with a prolonged Q-Tc interval could rheumatic fever be considered from the present illness, past history, family history or laboratory findings. The case of G. L. is briefly reported.

Case 2.—G. L., a 9 year old white boy, was admitted on Sept. 14, 1949 with fever and vomiting of three days' duration. He had had several nosebleeds during the current illness. His neck had been stiff for one day. Both upper and lower extremities were paralyzed, with severer involvement on the left. Spinal fluid findings confirmed the diagnosis of acute anterior poliomyelitis. An electrocardiogram made shortly after admission revealed a Q-Tc interval of 0.461 second.

18. Knies, P. T.: The Electrocardiogram in Induced Fever, Am. Heart J. **22**:804, 1941. Clagett, A. H., Jr.: Electrocardiographic Changes Following Artificial Hyperpyrexia, Am. J. M. Sc. **208**:81, 1944.

19. Freedberg, A. S.; McManus, M. J., and Altschule, M. D.: The Electrocardiogram in Man During an Episode of Chill and Fever Induced by Intravenous Typhoid Vaccine, Am. Heart J. **34**:249, 1947.

During the following twenty-four hours the temperature remained elevated and paralysis extended to involve the neck and back. The extremities were weaker, particularly on the left. The Q-Tc interval was 0.458 second. On September 16 the temperature was normal and a grade 1 systolic murmur was heard at the apex

Summary of Clinical and Electrocardiographic Observations

Patient	Age	Paralysis*	Heart	Q-Tc	Other Electrocardiographic Changes*
A. C.	11	None	Normal	P	Normal
R. D.	1	RA 4+; LA 4+; RL 4+; LL 4+; N; B; IC; RD	Marked tachycardia	P	Tachycardia
E. H.	13	RL 2+; LL 2+; LA 1+; Abd.	Tic-tac rhythm	P	RAD
G. L.	9	RA 2-3+; LA 2-3+; Transient IC; RL 3-4+; LL 3-4+	Grade 1 systolic murmur, left sternal border; tic-tac rhythm; evanescent sounds	P	Transiently prolonged PR interval
D. P.	7	None	Normal	P	Normal
J. M.	3	RL 2+; LL 3+	Normal	E	Normal
S. R.	1	RL 2+; LA 2+	Tachycardia	E	Tachycardia; slightly prolonged PR; notched RV
J. W.	13	None	Grade 2 basal systolic murmur	E	Normal
B. A.	1	RL 2+; LL 4+	Soft basal systolic murmur	N	Prominent R, V_1, V_2 and notched
N. B.	4	LA 2+; N; B	Normal	N	Normal
J. C.	6	None	Basal systolic murmur grade 4	N	Tachycardia; abnormal T waves
R. G.	5	Transient IC; shoulder girdle; B; Abd.	Normal	N	Normal
R. H.	12	None	Normal	N	RAD
R. L.	6	None	Grade 1 systolic murmur, left sternal border	N	Normal
R. M.	6	None	Normal	N	Normal
D. M.	3	RL 3+	Normal	N	Normal
P. M.	5	Transient Bu; RL 1+; LL 1+	Normal	N	Normal
J. O.	11	RL 3+; LL 2+; RA 1+; Mild Bu	Normal	N	Normal
C. O.	5	None	Grade 2 systolic murmur, left sternal border	N	Normal
B. P.	2	None	Normal	N	Tachycardia
P. R.	5	None	Normal	N	Normal
D. R.	1	RA 1+	Inconstant grade 1 basal systolic murmur	N	Normal
F. S.	3	None	Tachycardia	N	RAD; prominent R in V_1

* Explanation of symbols:

RA, right arm
LA, left arm
RL, right leg
LL, left leg
IC, intercostals
N, neck
B, back
Abd., abdominal
RD, right side of diaphragm
Bu, bulbar
1-4+, gross severity of paralysis
P, prolonged
E, equivocal
N, normal
RAD, right axis deviation

of the heart. There was definite tic-tac rhythm, and the Q-Tc interval was 0.453 second. The heart was not enlarged.

Thereafter, the patient gradually improved. The Q-Tc interval became shorter. Transient first degree heart block appeared between September 22 and October 1, after which the P-R interval remained normal. On the latter date, the systolic murmur could no longer be heard. The Q-Tc interval was 0.431 second. Fluoro-

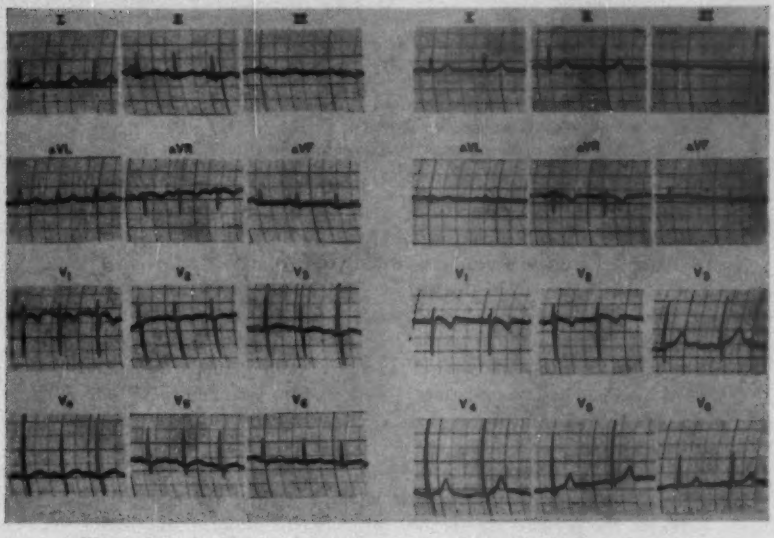

Fig. 1 (case 2).—Electrocardiogram showing the marked prolongation of the Q-T interval shortly after admission (Q-Tc, 0.458 second), compared with a completely normal tracing made fifty days later (Q-Tc, 0.407 second).

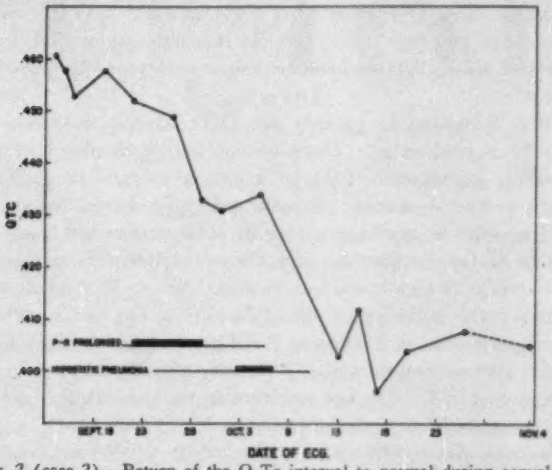

Fig. 2 (case 2).—Return of the Q-Tc interval to normal during convalescence from acute poliomyelitis. Note the transient prolongation of the P-R interval for age and rate.

scopic examination revealed fulness of the right auricle and some enlargement of the inflow tract of the right ventricle. On October 3 mild hypostatic pneumonia developed; it was treated and cleared three days later. The patient continued to improve slowly with physical therapy. On October 13 the Q-Tc interval was 0.403 second. The Q-Tc interval remained within the normal range until November 4, when the last electrocardiogram was made.

Illustrative electrocardiograms of this patient are seen in figures 1 and 2.

It appears that in this case the prolonged Q-Tc interval together with other positive findings pointing to involvement of the heart might indicate the presence of myocarditis.

The Q-Tc interval was considered equivocal in 3 patients (J. M., S. R. and J. W.). J. M. had a slightly prolonged Q-Tc interval (0.426 second; 5.2 per cent greater than 0.405 second) on one occasion. Five other tracings from this patient showed the Q-Tc interval to be within the normal range. This single abnormal measurement may not be of significance. S. R. had a maximum Q-Tc interval of 0.422 second (plus 4.2 per cent). However, during nine subsequent tracings made over a thirty-six day period the Q-Tc interval returned gradually and consistently to the normal level of 0.405 second. Slight transient prolongation of the P-R interval in three successive tracings supports the possible significance of consistent minimal lengthening of the Q-Tc interval in this case. J. W. showed slight lengthening of the Q-Tc interval on three tracings (up to 0.431 second), which was followed by two normal measurements (0.405 and 0.407 second). A fifth tracing had a Q-Tc interval of 0.424 second. J. W., however, is an adolescent girl (age 13). If adult standards are applied, the significance of these slight and inconsistent prolongations becomes highly improbable.

In the remaining 15 patients, the Q-Tc interval was consistently within the normal range. There was no significant difference in the incidence of prolongation of the Q-Tc interval in paralytic and in non-paralytic groups of patients. A prolonged Q-Tc interval did not occur more frequently in any subgrouping of paralytic patients according to extent or severity of paralysis, areas involved, presence or absence of signs of bulbar or high spinal involvement. Among 16 children 6 years or younger with poliomyelitis, the Q-Tc interval was prolonged in only 1 and was equivocal in 2. Among 7 children between the ages of 7 and 13 years with poliomyelitis, the Q-Tc interval was prolonged in 4 and was equivocal in 1. The age incidence in the cases and of the Q-Tc interval abnormalities is shown in figure 3.

No single electrocardiographic abnormality and no combination of abnormalities could be significantly related to any clinical aspect of acute poliomyelitis. Sex, race, duration of illness, fever, extent or severity of paralysis and occurrence of signs of bulbar or high cervical spinal

involvement were unrelated to the occurrence of abnormalities in the electrocardiogram. The occurrence of systolic murmurs and their loudness, location and transmission were similarly unrelated to electrocardiographic abnormalities. The clinical and electrocardiographic findings are summarized in the table.

Among 55 random control patients, marked sinus tachycardia was observed in two. There were no P wave abnormalities or prolongations of the P-R interval. Two patients had a definite right axis deviation. Four had a prominent R wave and/or a prominent R′ in lead V_1. There were no S-T or T wave abnormalities. One patient had occasional premature ventricular contractions with no evidence of cardiovascular disease. No patient had a significantly prolonged Q-Tc interval, although

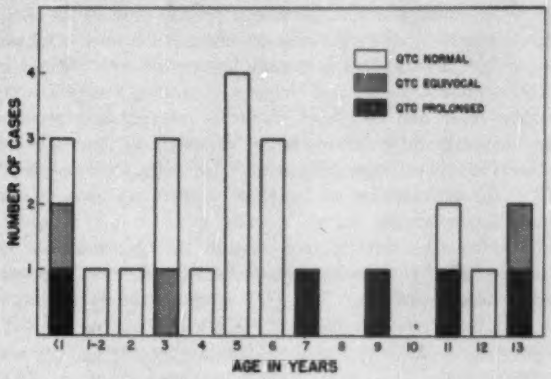

Fig. 3.—Age incidence in cases and of the Q-Tc abnormalities.

the Q-Tc interval was equivocal in 3 patients. No control patient had a Q-Tc exceeding the 5 per cent increment allowed over 0.405, with the exception of one measurement (0.431 second; plus 6.4 per cent), on a patient with a diagnosis of acute laryngotracheitis caused by Hemophilus influenzae.

COMMENT

Myocarditis is well known as a manifestation of rheumatic fever and as a complication of diphtheria. Rantz [1] has pointed out that in the absence of septicemia, however, other infectious diseases are rarely accompanied or followed by myocardial involvement leading to cardiac disability or unexpected death. Patients seriously ill with poliomyelitis may die suddenly and unexpectedly. The usual explanation is invasion by the virus and destruction of vital centers controlling respiratory and circulatory function. Nevertheless, clinical and pathologic studies

previously cited [20] have indicated that myocarditis in poliomyelitis may cause unexpected death. Determination of the extent to which lesions of the myocardium may influence the course of poliomyelitis awaits an accurate diagnostic technic, verified by clinicopathologic correlation.

In the present study, we were unable to make the diagnosis of myocardial embarrassment consistently or with certainty by clinical observation alone. Suggested clinical criteria include changes in blood pressure, sudden or disproportionate tachycardia or bradycardia, tic-tac rhythm, changing quality of heart sounds and murmurs, diminished intensity of the first heart sound in the mitral area, transient arrhythmias, signs of pulmonary edema, cardiac decompensation and shock.[21]

Gefter and associates [12] pointed out that the electrocardiogram was of greater value than clinical evaluation in detecting the presence of carditis. They found that carditis might be suspected from abnormal electrocardiographic findings but that the changes observed were neither uniform nor specific. This is in general agreement with Neubauer's [18a] earlier observations. Taran and Szilagyi [16a] studied the Q-Tc interval in rheumatic fever and concluded that this measurement furnished a sensitive diagnostic aid in the detection of active carditis. This study has been verified recently by Abrahams,[16b] although Pokress and Goldberger [22] found prolongation of the Q-Tc interval in acute rheumatic fever somewhat inconstant.

Factors other than carditis may lengthen the Q-T interval. These include excitement, hypocalcemia, hypokaliemia, quinidine, hypertension and cardiac decompensation. The Q-T interval may be shortened by digitalis, salicylates or hypercalcemia. Taran [16] has pointed out that marked shortening of the Q-T interval may also occur with pericarditis. Measurement of the Q-T interval may be variable and unreliable in the presence of a cardiac arrhythmia other than respiratory sinus arrhythmia. Interpretation of changes in the Q-Tc interval must include an evaluation of such variables.

The Q-Tc interval was prolonged in 5 (21.7 per cent) of 23 patients with acute poliomyelitis in the present series and was considered equivocal in 3 patients (13.0 per cent). The Q-Tc interval was equivocal in 3 patients (5.4 per cent) in a control series of 55 patients and was prolonged in none. The difference between measurements of the Q-Tc interval in these two groups of patients is statistically significant. In a current series of observations on rheumatic fever we have seen no case of active carditis uncomplicated by definite pericarditis or by digitalis

20. Saphir and Wile.[6] Peale and Lucchesi.[7] Saphir.[9] Ludden and Edwards.[10] Boucek, Bailey, Burchell and Edwards.[11]

21. Gore.[8] Neubauer.[18a]

22. Pokress, M. J., and Goldberger, E.: A Study of the Q-T Interval in Rheumatic Fever, Am. Heart J. **38**:423, 1949.

or salicylate therapy in which the Q-Tc interval has not been prolonged. The unusually frequent occurrence of a prolonged Q-Tc interval in the present series of patients with poliomyelitis raises the question of the diagnostic significance of the measurement in evaluating myocardial integrity in patients with infectious disease. The answer must await more extensive clinical study correlated with histologic observations.

Other electrocardiographic changes noted were not of specific diagnostic value. Minor and transient abnormalities, which may be due to poorly defined functional derangement of no clinical importance, should not be given undue emphasis in diagnostic interpretation in the absence of supporting clinical or electrocardiographic evidence of myocardial disease.

It is planned to extend the present studies in an effort to evaluate cardiac status more clearly during and following acute poliomyelitis. Pathologic material which becomes available will be compared with the clinical and electrocardiographic data in future studies.

SUMMARY

Electrocardiographic studies on 23 patients with acute poliomyelitis are reported. The Q-Tc interval was prolonged in 5 patients and was equivocal in 3. In a control series of 55 patients, the Q-Tc interval was equivocal in 3. The possible diagnostic significance of the Q-Tc interval is discussed, and the need for further clinical and pathologic study is cited. No other electrocardiographic abnormality noted was of specific diagnostic significance.

ADDENDUM

After we had prepared this manuscript, Bradford and Anderson [23] reported electrocardiographic abnormalities in 12 per cent of 155 patients with poliomyelitis. These included evidence of right ventricular strain, S-T segment and T wave abnormalitties and conduction disturbances. In 4 of 5 fatal cases there were significant electrocardiographic changes, but pathologic findings were inconclusive. No study of the Q-T interval was included.

Strong Memorial Hospital.

23. Bradford, H. A., and Anderson, L. L.: Electrocardiographic Observations During a Poliomyelitis Epidemic, Ann. Int. Med. **32**:270, 1950.

ANOXIA AS A CAUSE OF FETAL DEATH AND CONGENITAL DEFECT IN THE MOUSE

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RICHARD A. PRINDLE, M.D.
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THAT anoxia at critical stages of prenatal development is an important cause of acquired malformations of the fetus is an inference derived from earlier studies of mongolism, retrolental fibroplasia and tracheoesophageal fistula.[1] This hypothesis has been tested experimentally by submitting pregnant mice at various stages of gestation to rarefied atmospheres.

MATERIALS AND METHODS

The white mouse is a prolific, easily handled mammal in which the onset of pregnancy can be determined with much certainty by means of an inspissated plug appearing in the vagina shortly after copulation. Females used were chosen at random from a laboratory strain maintained for the past four years with avoidance of brother and sister mating. Fertility has remained satisfactory, with a mean of 8.2 normal pups per litter. For the purposes of these experiments the day on which the copulation plug appears is regarded as the first day of pregnancy, and it is our practice to deliver the uterine contents by surgical section on the eighteenth day. The operation terminates the life of all fetuses but permits accurate count of blighted embryos, which otherwise probably would escape notice.

The anoxic insult was administered to pregnant mice within the confine of a bell jar, as shown in figure 1. During an experiment a vacuum pump continuously exhausts the bell jar while entrance of air into the system is restricted by means of the adjustable globe valve indicated by the arrow in the first figure. Equilibrium is established at a selected atmospheric pressure below 240 mm. of mercury, which

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1. Ingalls, T. H.: Etiology of Mongolism; Epidemiologic and Teratologic Implications, Am. J. Dis. Child. **74**:147 (Aug.) 1947; Congenital Encephalo-Ophthalmic Dysplasia: Epidemiologic Implications, Pediat. **1**:315, 1948; Epidemiology of Encephalo-Ophthalmic Dysplasia, J. A. M. A. **138**:261 (Sept. 25) 1948. Ingalls, T. H., and Prindle, R. A.: Esophageal Atresia with Tracheo-Esophageal Fistula: Epidemiologic and Teratologic Implications, New England J. Med. **240**:987, 1949.

roughly corresponds to a 30,000 foot (9,150 meter) ceiling that cannot be tolerated for long by the mother. Under conditions of the experiment, the dosage factor (i. e., degree and duration of relative anoxia) may be controlled and quantitated, while the continuous flow of over 3 liters of air a minute through the system prevents asphyxia. A water bottle, added to the circuit, serves to standardize the humidity and temperature of the air. Under such conditions, as was shown by the pioneer investigations of Paul Bert [2] and confirmed repeatedly in recent years,[3] the physiologic insult is primarily one of anoxic anoxia provided that reduction of atmospheric pressure is so gradual as to avoid causing bends. Our practice has been to set the time for decompression and recompression at about fifteen minutes.

Fig. 1.—High altitude chamber constructed from bell jar. During an experiment air is continuously being exhausted from the system by vacuum pump with entrance of air restricted by means of adjustable globe valve marked with an arrow. The water bottle serves to standardize humidity and temperature of the air.

2. Bert, P.: Barometric Pressure: Researches in Experimental Physiology, Columbus, Ohio, College Book Co., 1943.

3. (*a*) Monge, C.: Chronic Mountain Sickness, Physiol. Rev. **23**:166, 1943. (*b*) Altland, P. D.: Breeding Performance of Rats Exposed Repeatedly to 18,000 Feet Simulated Altitude, Physiol. Zoöl. **22**:235, 1949. (*c*) Highman, B., and Altland, P. D.: Acclimatization Response and Pathologic Changes in Rats at an Altitude of 25,000 Feet, Arch. Path. **48**:503 (Dec.) 1949. (*d*) Altland, P. D.: Effect of Discontinuous Exposure to 25,000 Feet Simulated Altitude on Growth and Reproduction of the Albino Rat, J. Exper. Zool. **110**:1, 1949.

To date, 65 mice with copulation plugs have been exposed at various stages of pregnancy to an atmospheric equivalent of an altitude of approximately 27,000 feet (260 mm. of mercury) for five hours at room temperature (23 to 25 C.); another group (68 mice) has been similarly exposed at a simulated altitude of about 25,000 feet (280 mm. of mercury) and a third group (60 mice), serving as control animals, has been maintained without change at sea level (760 mm. of mercury).

RESULTS

Among the control animals, 51 produced 443 embryos and 9 (15 per cent) produced no young at all after appearance of the copulation plug (table). Of the 443 verified conceptions, 27 (6.1 per cent) were blighted in utero, as evidenced by the presence of placental remnants in

Results of Pregnancy in Sixty Control Mice with Copulation Plugs

Number of Embryos	Observed Frequency	Status of Embryos: Normal, No.	Status of Embryos: Abnormal, No.	Status of Embryos: Abnormal, %
0	9	0	0	....
1	0	0	0	....
2	2	4	0	....
3	0	0	0	....
4	1	4	0	....
5	1	5	0	....
6	1	6	0	....
7	3	21	0	....
8	12	103	1	0.97
9	16	134	10	6.94
10	5	46	4	8.00
11	5	49	6	10.90
12	2	22	2	8.33
13	2	22	4	15.38
Totals	60	416	27	6.09
Mean number of embryos *	..	6.9	0.45	....

* Included in the computation were 9 mice in which no evidence of conception was found following appearance of copulation plugs.

the uterus. Since the percentage incidence of blighted embryos is greater as litter size rises, the interpretation is advanced that most losses among control animals may be attributed to uterine crowding. A progressive increase in intrauterine fatality is characteristic of twin, triplet and quadruplet siblings in human births.[4]

A significant reduction in mean number of normal embryos occurred among litters of mice exposed to high altitude anoxia compared with controls producing 6.9 normal embryos per copulation plug, as shown in figure 2. The mean number of embryos arranged according to day of gestation on which maternal anoxia was sustained are shown for insults

4. Newman, H. H.: Multiple Human Births: Twins, Triplets, Quadruplets and Quintuplets, New York, Doubleday, Doran & Company, 1940.

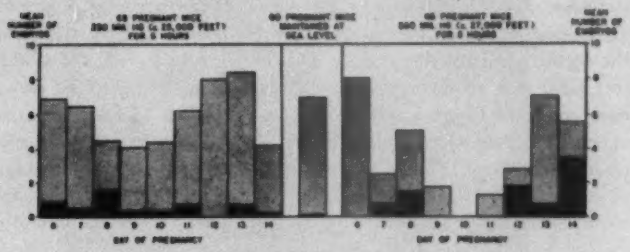

Fig. 2.—Number of embryos following maternal anoxia by day of pregnancy and altitude. Cross-hatched columns, normal embryos; black columns, abnormal embryos.

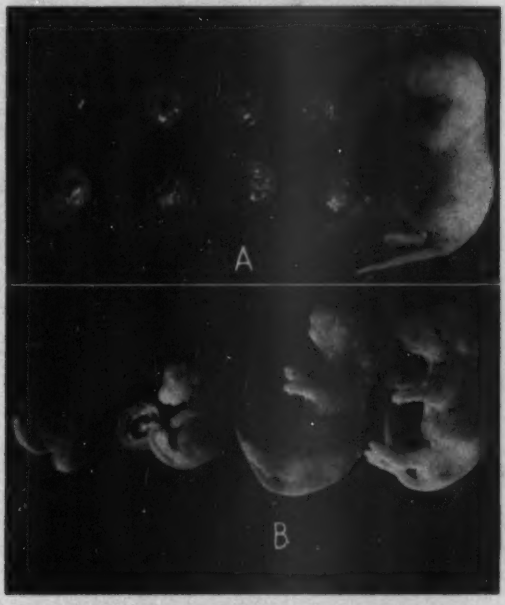

Fig. 3.—*A*, uterine contents of mouse subjected to simulated altitude of 27,000 feet for five hours on twelfth day of gestation. One normal-appearing fetus survived. *B*, uterine contents of mouse subjected to simulated altitude of 27,000 feet for five hours on thirteenth day of gestation. Seven normal-appearing fetuses are not shown.

administered between the sixth and fourteenth days of pregnancy, inclusive. At 25,000 feet (280 mm. of mercury) an appreciable diminution in number of embryos found is evident following anoxia on the eighth, ninth and tenth days. This is markedly accentuated at 27,000 feet (260 mm. of mercury), so that on the ninth, tenth and eleventh days only 2 of 12 animals produced litters totaling 12 embryos, normal expectancy being 83. The uteri of the other 10 mice were void of even a placental remnant. These findings are consistent with the observation of Altland [8d] that female rats, although housed with fertile males, failed to reproduce when exposed daily for four hours to simulated altitudes

Fig. 4.—Uterine contents of mouse subjected to simulated altitude of 27,000 feet for five hours on the fourteenth day of gestation.

of 25,000 feet. If single exposures for five hours at altitudes of 25,000 feet or higher frequently register lethal effects on the unborn young, it is not surprising to find that daily exposures are totally destructive.

The products of gestation observed in this study range through a complete spectrum or biologic gradient, from small placental remnants (fig. 3*A*), with or without absorbed fetal components, through gross fetal defects (fig. 3*B*) and monstrosities to normal-appearing pups. Criteria of abnormality for the purposes of these experiments are those which are recognizable macroscopically (figs. 4 and 5) and those defects which can be identified in the stained skeleton (figs. 6 and 7) after clearing and mounting in plastic according to a previously described

Fig. 5.—Uterine contents of mouse subjected to simulated altitude of 27,000 feet for five hours on the eighth day of gestation.

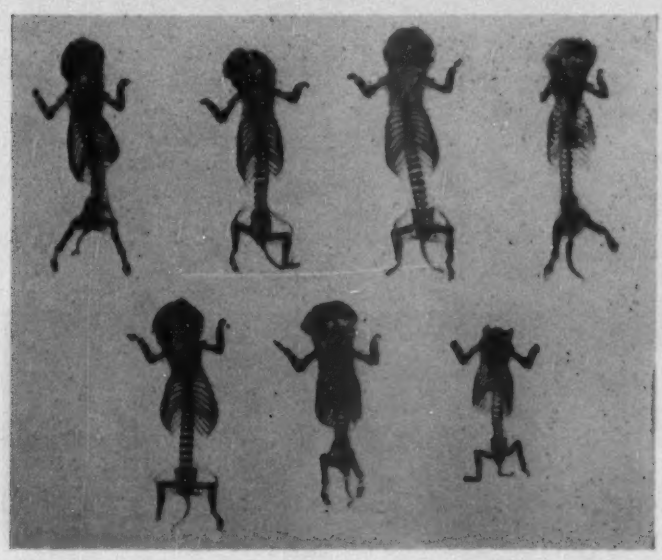

Fig. 6.—Uterine contents of mouse subjected to simulated altitude of 25,000 feet for five hours on the eighth day of gestation. Skeletons have been cleared and stained to show anencephalic member.

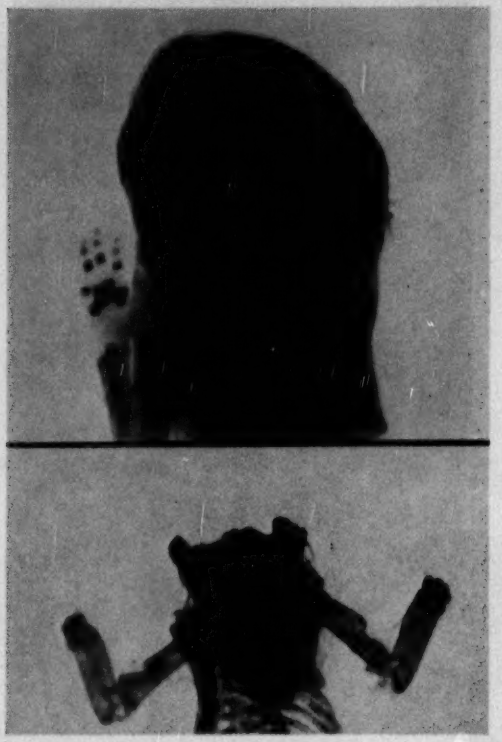

Fig. 7.—Anencephalic member (fig. 6) shown in greater detail, compared with a normal skull.

Fig. 8.—Cleft palate in 2 members of the litter, shown in figure 4.

method.[5] This method, although excellent for the study of skeletal detail, has been used sparingly, since the specimen is lost for histologic examination of stained sections. Detailed studies of the various organ systems have not yet been made, and it is probable that anomalies exist which have not been detected.

Although the congenital anomalies which have been recognized were, as a rule, of a severity incompatible with life, 9 instances of cleft palate

Fig. 9.—*A*, uterine contents of mouse subjected to simulated altitude of 25,000 feet for five hours on the eighth day of gestation, showing a placental remnant, an anencephalic, a normal and 2 dwarfed fetuses. Six normal-appearing fetuses are not shown. *B*, uterine contents of mouse subjected to simulated altitude of 25,000 feet for five hours on the eighth day of gestation. Seven normal-appearing fetuses are not shown.

(fig. 8) were found among progeny of 3 mice subjected to anoxic insult on the fourteenth day of gestation. The finding harmonizes with the

5. Ingalls, T. H.: Congenital Malformations in Research in Medical Science, New York, The Macmillan Company, 1950.

Fig. 10.—Frontal section at the plane of the eyes of the skulls of the 2 mice (anencephalic top, normal bottom) shown in figure 9 *B*.

observation of Warkany [6] that a critical stage exists in the 13 or 14 day old rat embryo at which the absence of riboflavin may determine the development of cleft palate. The most interesting anomaly which repeated itself was anencephaly (figs. 9 and 10), found once in each of three litters of mothers exposed at 25,000 feet on the eighth day of gestation. The probability that all three litters would fortuitously contain such a member after a maternal insult on any particular day is less than 1 to 5,000. These odds suggest that anencephaly, like cyclopia in the fish [7] and cleft palate in the rat,[6] is stage specific in the sense that it can arise only at some critical phase of cephalic development.

COMMENT

The French scientist, Geoffroy Saint-Hilaire, in his classic treatise on anomalies, published in 1837,[8] described anencephaly as an acquired arrest of cranial development. Forty years later his countryman Camille Dareste reported the artificial production of monstrosities, including anencephaly in the chick embryo, following thermal insults of the embryonating egg.[9] One of the principal contributions of Saint-Hilaire, stated Dareste, "is the concept that the biggest monster and smallest anomaly are essentially facts of the same order—deviations from a specific type produced by altering development. Only, monstrosities involve profoundly and simultaneously a large number of organs. The difference between these two sorts of facts results basically from the difference in the intensity of the modifying cause and perhaps also from the time of their action." In our experiments on white mice, the monsters (e. g., anencephaly—figs. 6, 7 and 9), the anomalies (e. g., cleft palate, fig. 8) and the fetal deaths are interpreted as "facts of the same order" with differences determined by the severity, not the kind, of maternal illness.

Differences in the intensity of the modifying cause, anoxic anoxia, determine not only the frequency of embryonic deaths, as shown in figure 2, but also the kind of abnormal embryos. Anencephaly, for example, followed exposures to simulated atmospheres of 25,000 feet and was not found among progeny of animals exposed at 27,000 feet or maintained at sea level.

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6. Warkany, J.: Manifestations of Prenatal Nutritional Deficiency, Vitamins & Hormones **3**:73, 1945.

7. Stockard, C. R.: Development of Artificially Produced Cyclopean Fish—"The Magnesium Embryo," J. Exper. Zool. **6**:285, 1909.

8. Geoffroy Saint-Hilaire, I.: Des anomalies, Paris, 1837.

9. Dareste, C.: Recherches sur la production artificielle des monstruosités ou essais de tératogénie expérimentale, Paris, C. Reinwald & Co., 1877, p. 39.

Likewise, the influence of timing of the maternal insult is clearly discernible in the causation of intrauterine deaths and congenital deformities. Specific effects depend on the stage of fetal development and the sites involved when maternal disease occurs. Anencephaly of the fetus results from systemic anoxia, assuredly with focal involvement of cephalic structures, on the eighth day of gestation. It is reasonable to infer that certain rapidly differentiating cephalic structures are more vulnerable to anoxia on that day than resting cells or fully differentiated tissues. To reconstruct fully the pathogenesis of anencephaly and other acquired anomalies consequent to anoxia, a series of embryos must be studied during early periods of reactivity and repair.

A third factor influencing the frequency of blighted embryos, and possibly of acquired anomalies, is litter size. Among the control animals, as the number of members in a litter increased so, too, did numbers of placental remnants indicative of embryonic deaths. The importance of this unexpected finding as an ancillary cause of acquired anomalies following maternal anoxia remains to be evaluated with a larger number of animals than thus far studied. The nature of future problems which await solution by the experimental approach begins to take shape. What, for example, is the complete pattern of potential deviations from normal development after ten hours' exposure to 25,000 feet of altitude on the eighth day of gestation when the number of fertilized ova is ten? Would a similar pattern result from longer exposures at lower altitudes? What is the relation between cleft palate produced in rodents by anoxia and that described by Warkany as resulting from dietary deficiencies[8] or by the Gillmans from parental injection of trypan blue[10]? Such questions may be answered by appropriate experiments under fixed conditions resulting in the repeatable production of anomalies. As a point of departure, these investigations have shown that it is possible to control and quantitate in adequate detail dosage factor, timing and duration of anoxia as a teratogenic agent; to evaluate actions on and the reactions of both maternal and fetal organisms, and to define intermediate stages which intervene between the acute maternal insult and resulting fetal deaths and congenital anomalies.

CONCLUSIONS

1. Maternal anoxia may result in fetal death or congenital deformity in the mouse.

2. The effect on the conceptus varies with the degree of maternal-placental anoxia and the stage of gestation at which the anoxic insult occurs.

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10. Gillman, J.; Gilbert, C., and Gillman, T.: A Preliminary Report on Hydrocephalus, Spina Bifida and Other Congenital Anomalies in the Rat Produced by Trypan Blue, South African J. M. Sc. **13**:47, 1948.

3. The effect registered on the fetus is assuredly determined also by anatomic characteristics of the site at which localized cellular damage occurs, and the hypothesis is advanced that rapidly differentiating tissues are more vulnerable to anoxia than resting or fully differentiated cells.

4. A method has been perfected which permits systematic evaluation of roles played by a teratogenic agent, the fetal host and the maternal placental environment in the production of acquired congenital anomalies.

LARVAL ASCARIASIS AS A CAUSE OF CHRONIC EOSINOPHILIA WITH VISCERAL MANIFESTATIONS

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A SYNDROME has recently been described [1] which is characterized by chronic eosinophilia and eosinophilic granulomatous lesions of the liver associated with fever, leukocytosis, hyperglobulinemia and pulmonary changes. This syndrome has been related to the group of disorders characterized by eosinophilia and pulmonary changes which include Löffler's syndrome [2] and tropical eosinophilia.[3]

The etiologic basis of this syndrome has not been proved, but it has been assumed to represent an allergic response to unknown antigens with the liver acting as a "shock organ." [1b] In one report the antigen is assumed to be a toxin from the helminth Ascaris lumbricoides.[1a]

A patient with the aforementioned clinical entity in whom the basic etiologic mechanism could be clearly demonstrated was recently studied in this clinic. The hepatic lesions were found to be caused by the presence within that organ of the larvae of A. lumbricoides. This patient's case is presented in the belief that this or a similar mechanism should possibly be considered in other examples of this syndrome.

From the Departments of Pediatrics, Pathology and Microbiology, Western Reserve University.

1. (*a*) Perlingiero, J. G., and György, P.: Chronic Eosinophilia: Report of a Case with Necrosis of the Liver, Pulmonary Infiltrations, Anemia and Ascaris Infestation, Am. J. Dis. Child. **73**:34 (Jan.) 1947. (*b*) Zuelzer, W. W., and Apt, L.: Disseminated Visceral Lesions Associated with Extreme Eosinophilia: Pathologic and Clinical Observations on a Syndrome of Young Children, Am. J. Dis. Child. **78**:153 (Aug.) 1949.

2. (*a*) Löffler, W.: Successive Transient Pulmonary Infiltrates with Eosinophilia, Beitr. z. Klin. d. Tuberk. **79**:368, 1932; (*b*) Transitory Pulmonary Infiltrates with Eosinophilia, Schweiz. med. Wchnschr. **66**:1069, 1936.

3. Frimodt-Möller, C., and Barton, R. M.: A Pseudotuberculous Condition Associated with Eosinophilia, Ind. M. Gaz. **75**:607, 1940. Weingarten, R. J.: Tropical Eosinophilia, Lancet **1**:103, 1943.

REVIEW OF THE LITERATURE

The syndrome of chronic eosinophilia and eosinophilic granulomatous lesions of the liver associated with fever, leukocytosis, hyperglobulinemia and pulmonary changes was first described by Perlingiero and György in 1947.[1a] Their patient was a 2 year old Negro boy with a known allergic background, who had lived in Florida and was known to have ingested large quantities of "dirt." A biopsy of his enlarged liver showed lesions characterized by a focal necrosis, with infiltration of neutrophilic and eosinophilic leukocytes. These authors were not able to find ova or parasites in the liver biopsy specimen, sputum, bronchial secretions, duodenal drainage or feces. However, the patient vomited a single adult male ascaris, after which he improved remarkably. The authors found it not difficult to assume that all the lesions could well be explained on the basis of an allergic response to ascaris "toxin."

Zuelzer and Apt in 1949 [1b] described a group of cases characterized by eosinophilia of the blood and bone marrow, leukocytosis and hyperglobulinemia persisting over long periods. The clinical manifestations were variable, and among them were hepatomegaly, pulmonary infiltrations, asthmatic complaints, articular symptoms, urticaria and convulsions. What was evidently a lesion identical with that described by Perlingiero and György was found at autopsy in 1 case and at biopsy in 3 others. In no instance were these authors able to demonstrate the presence of ascaris, and there was no evidence of sensitivity to the common parasitic antigens. The lesions were interpreted as an "allergic-hyperergic" tissue response to undetermined antigens.

A search of the literature revealed only 2 other reports of eosinophilia associated with focal lesions in the liver. One, by Thomson, Wilson and McDonald in 1937,[4] described the lesions as being similar to those seen in tularemia. The other, described by Atmar in 1940,[5] concerned a patient whose disease this author regarded as presenting an example of familial eosinophilia.

No reports have been found which described ascaris larvae in the liver of the human being.

REPORT OF A CASE

History.—B. K., a 2 year old white girl, was entirely well until five months prior to admission to this hospital. At that time her mother noted that she became irritable and lethargic, refused to run about and play as usual and manifested anorexia to the point where she refused all solid foods and would drink only milk

4. Thomson, A. P.; Wilson, G. H., and McDonald, S.: Three Cases of Unusual Illness with Eosinophilia: One with Lesions in Liver Resembling Those of Tularemia, Lancet **2**:9, 1937.

5. Atmar, R. C.: Familial Eosinophilia: Report of a Case with Biopsy of Liver, J. A. M. A. **115**:449 (Aug. 10) 1940.

and soup. The mother also noted a mild, constant fever. In addition, headaches and vague abdominal pains developed in the patient. Three months prior to admission the child refused to walk and insisted on being carried from place to place. She was admitted to another hospital in which, during a three weeks' stay, she received treatment with liver, vitamin B_{12} and transfusions of whole blood. Shortly thereafter, she began to complain constantly of a pain in the upper part of her abdomen. Her abdomen became progressively distended, and there were increasing pallor and weakness with marked sweating both night and day. One episode of vomiting occurred. The mother described the material vomited as "tomato-colored." At the same time red-tinged stools were passed. All symptoms persisted to the time of admission, and there was a slight loss of weight over the five month period.

The past history revealed that the patient had been born two months prematurely. She weighed 2,000 Gm. and was placed in an incubator for five weeks. At birth a lesion on the inner aspect of the right thigh was noted, which was diagnosed as a cavernous hemangioma and was subsequently treated with irradiation. The child was never immunized. She was the second born of a father with Rh-positive blood and a mother with Rh-negative blood. The mother had an allergic eczema. The remainder of the history taken at the time of admission was not remarkable.

Physical Examination.—The child on admission was a well developed, well nourished white girl appearing somewhat pale and markedly irritable. An irradiation scar was noted on the inner aspect of the right thigh. Her temperature was 37.9 C (100.2 F.). A few shotty inguinal nodes were palpated. The rest of the abnormal physical conditions were limited to the abdomen, which was grossly distended, with a marked prominence of the superficial veins. There was no fluid wave or dulness in the region of the flank. The liver extended 5 cm. below the right costal margin, with a hard smooth edge extending well into the left upper quadrant. The spleen extended 7 cm. below the left costal margin and was firm, with a smooth margin. The rest of the abdominal distention appeared to be due to gas-filled loops of bowel.

Laboratory Data.—Laboratory findings revealed a hemoglobin content of 6.2 Gm., a red blood cell count of 3,700,000 and a white blood cell count of 38,000 with 62 per cent eosinophils. The total serum protein was 6.98 Gm., with such a large portion of that figure globulin that it was impossible to determine the amount of albumin present. The result of a cephalin flocculation test was 3+ in twenty-four hours and 3+ in forty-eight hours. Stools were examined repeatedly for ova and parasites but none were found. The results of tuberculin, histoplasmin and trichinella skin tests were negative. An aspiration of bone marrow showed marked eosinophilic hyperplasia. Roentgenograms of the chest showed infiltration in the upper lobe of the right lung and increased hilar markings with an area of miliary infiltration at the base of the right lung (fig. 1).

Microscopic Observations.—A biopsy of the liver was performed. At the time of operation the liver was enlarged, coarsely granular and deep red, exhibiting both discrete and confluent light tan foci which were firmer than the surrounding tissue and measured 0.5 to 2.0 mm. in diameter.

The biopsy specimen of the liver measured about 1.5 by 0.5 by 0.5 cm. Routine hematoxylin and eosin stains were made. After identification of larvae in preliminary sections, an unsuccessful attempt was made to identify them in cleared tissue. After this attempt, the tissue was reembedded and serial sections were made.

The conspicuous feature of all sections was the presence of foci of inflammation. These were disposed at random in the hepatic tissue. In some places they consisted

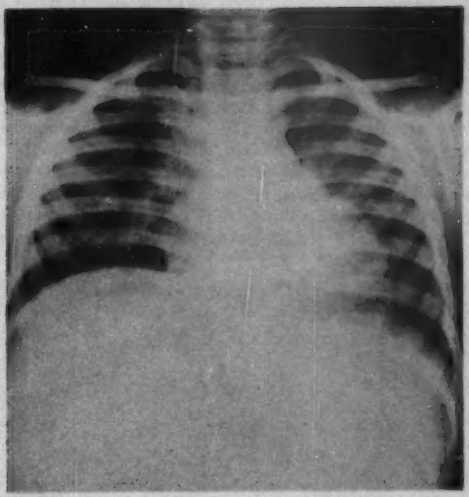

Fig. 1.—Roentgenogram of the chest on admission. Note increased density in the upper lobe of the right lung.

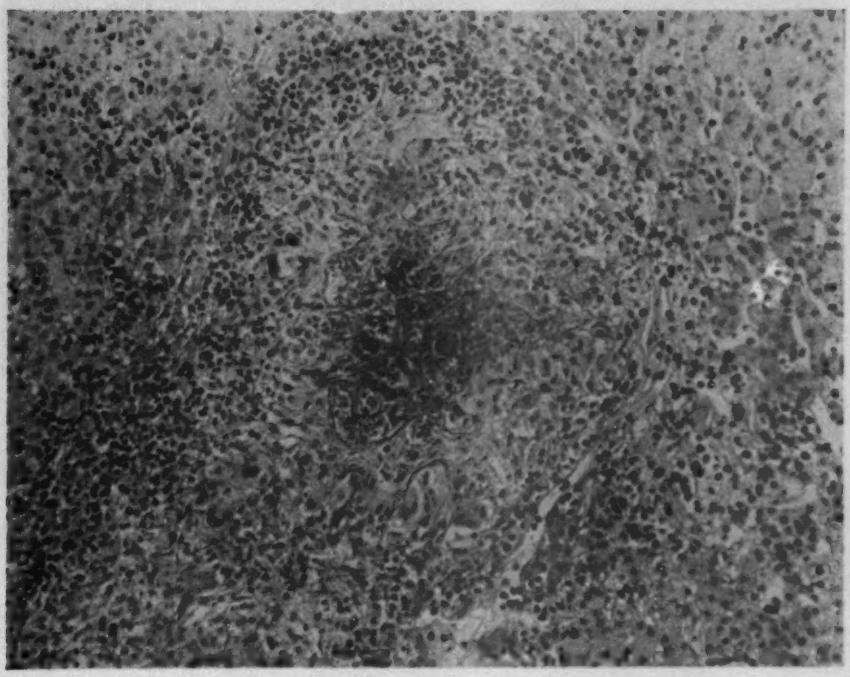

Fig. 2.—Granuloma in the liver. The fine black lines are intensely acidophilic. × 180.

entirely of eosinophils and plasma cells with a few phagocytes containing brown pigment. This was a purely exudative reaction. In other places the inflammatory foci were granulomatous (fig. 2) and consisted of a deeply acidophilic, fibrillar and granular center surrounded by a zone of polyhedral and fusiform cells. These cells were very large; they had oval nuclei, sometimes with nucleoli. There was a delicate chromatin network. The cytoplasm was very slightly acidophilic. In places it was homogeneous. In other places, especially along the borders of the cells, it contained acidophilic fibrils similar to those in the necrotic center. Sometimes there was a stippling of acidophilic material. In places there were giant

Fig. 3.—Focus of exudative inflammation in the liver, in which there is a larva (arrow). The larva is curled and therefore does not appear in its entirety in one plane of the section. × 420.

cells with a similar type of nucleus and cytoplasm. The nuclei were usually overlapping. They tended to have a peripheral distribution. The giant cells contained and enclosed the acidophilic fibrils and sometimes leukocytes. There was usually a variable admixture of eosinophils and plasma cells in these granulomatous foci. The exudative and granulomatous foci were not sharply defined from each other and were occasionally seen to merge, forming bands of inflammation with a progressively transitional appearance.

In all, four larvae were identified (fig. 3). Three of these were found in the preliminary sections, and only one was found in the serial sections. They were in

the exudative foci only. The larva found in the serial study was complete in two 10 micron sections. It was cut slightly obliquely and measured about 110 by 20 microns. It had pointed ends, one of which was slightly curved. The larvae showed a peripheral faintly refractile layer with scattered small oval nuclei and a central zone of overlapping small oval nuclei and faint basophilic granules.

The inflammatory foci occupied about one third of the hepatic tissue. The breadth of the foci varied from about one fourth to one half of the diameter of a lobule. Since the purely exudative reaction occurred around the larvae, it was assumed that this represented the acute reaction to invasion. The granulomatous foci represented older lesions. The keratin-like material present in the granulomas may have represented moult or dead larvae. However, the presence of necrotic larvae was not convincingly demonstrated.

In view of the fact that the exudative and granulomatous types of inflammation could be shown to be continuous in some instances, it may be that the lesion was actually a burrow. The more acute reaction was present in the forepart of this burrow around the larva itself, and the granulomatous reaction was in the distal part of the burrow around the keratin-like material shed by the larva. The final answer must await serial section reconstruction.

Around the central vein and often present in its wall and lumen there were eosinophilic leukocytes. Rarely, there was moderate fibroblastic proliferation beneath the intima. Eosinophils were scattered in the sinusoids, which were often distended but bloodless. In some places faintly stained material was seen in the sinusoids, but more frequently they appeared empty. Eosinophils and plasma cells were present to a variable degree around the periportal structures. Sometimes the leukocytes were seen in the walls and in the lumens of the tributaries of the portal vein.

The hepatic cells were foamy, indicating a rich storage of glycogen. The liver tissue ended rather abruptly at the margins of the inflammatory foci. A few hepatic cells were isolated by the exudative reaction, but they were not seen in the granulomatous foci.

Hospital Course.—Just prior to operation the patient passed a 6 inch (15 cm.) male A. lumbricoides per rectum. In the ten days following operation, she was given three separate courses of hexylresorcinol, 0.45 Gm. for each course. Each was followed with a purgative and an enema, and all stools that were passed were examined carefully for both worms and ova. Neither was found. She was given a transfusion of 500 cc. of whole blood and placed on a high protein diet supplemented with vitamins, yeast and iron.

Follow-up.—Two weeks after discharge the child returned to the hospital for reevaluation. The interim was marked by improvement in both her appetite and her disposition and a persistent, slightly productive, chesty cough. Physical examination revealed the spleen to be still easily palpable 3 cm. below the left costal margin and the liver 3 cm. below the right costal margin. A few harsh breath sounds were heard in the right pulmonary field and a few coarse rhonchi in both pulmonary fields. Stools were again free from ova and parasites. Roentgenograms of the chest still showed a prominence of the right hilus extending into the right superior mediastinum and a possible infiltrative process in the right cardiophrenic angle. An aspiration of bone marrow showed a persistence of eosinophilic hyperplasia. Pertinent laboratory findings are listed in the accompanying table. The child was given her fourth course of hexylresorcinol and discharged on the same regimen as outlined previously.

She was readmitted two months after the date of her initial admission, with a recurrence of irritability and abdominal distention. However, until a week prior to this admission the mother had noted a further improvement in her daughter's

appetite, disposition and activity. The child again became irritable and her abdomen became distended. Her cough was still present, although decreased in severity, and some noisy breathing was noted. Examination at this time showed a child still irritable and chronically ill. There had been an increase in the inguinal adenopathy. There was a slight decrease in resonance in the right upper pulmonary field, and auscultation revealed coarse inspiratory and expiratory rhonchi throughout both pulmonary fields. The abdomen was slightly distended, and both the liver and the spleen were increased in size. The spleen extended 4 cm. below the left costal margin and the liver 4 cm. below the right costal margin. The latter had become tender. Roentgenograms revealed increased prominence of the shadow in the right upper pulmonary field adjacent to the mediastinum but decreased prominence of the streaky and mottled densities in the midportion of the right lower pulmonary field. Antihistamine therapy was prescribed, and the clinical picture during the fourteen day hospital course was one of steady improvement. Her irritability disappeared, and she began playing with the other children in the ward. At the time of discharge her liver was still palpable 1 cm. below the right costal margin, and it was no longer tender. The spleen was also 1 cm. below the left costal margin.

Summary of Blood Studies Since First Admission

Date	White Blood Cells, No.	Eosinophils, %	Total Protein, %	Albumin, %	Globulin, %	Albumin-Globulin Ratio	Cholesterol, Mg./100 Cc.	Cholesterol Esters, Mg./100 Cc.	Total Lipid, Mg./100 Cc.	Cephalin Flocculation, 24 Hr.	Cephalin Flocculation, 48 Hr.	Thymol Turbidity, Units	Icterus Index	Alkaline Phosphatase, Bodansky Units	Phosphorus, Mg./100 Cc.
11/16	38,000	02	6.96	....	6.08	....	...	....	...	3+	3+	...	...	11.6	5.18
11/26	37,000	01	6.07	3.34	3.63	0.92	...	....	...	1+	3+	...	6	7.1	5.87
12/2	39,000	02	7.3	2.8	4.5	0.62	119	69	310	1+	3+	...	...	6.8	5.89
12/22	24,000	02	8.55	3.14	5.41	0.56	126	87.4	505	2+	...	4.5	4	10.73	5.27
1/16	21,000	72	6.45	2.02	3.43	0.89	123	88.7	480	3+	3+	4.6	3.5	12.9	4.81
1/27	17,300	57	7.7	3.67	4.03	0.91	...	....	530	2+	3+	...	3.7	8.2	5.3
Normal	10,000	1-3	6.5-8.0	4.5-5.5	1.8-2.5	1.7-3.0	70-200	125-150	500-700	0	0	...	4-6	5-13	4.5-5.5

Roentgenograms of the chest on discharge revealed a clearing of all pulmonary infiltration but a persistence of the heavy bronchovascular markings in the right hilus extending into the right lower pulmonary field (fig. 4). The right upper pulmonary field had cleared completely. (The laboratory data on this admission are shown in the accompanying table.) The child was discharged on her fourteenth hospital day to continue with the antihistamine therapy at home, as well as with her high protein diet and supplements of yeast and vitamins. An ascaris skin test performed in the clinic after this discharge was strongly positive.

In view of the definite evidence of the presence of ascariasis, it was deemed advisable to consult with the family of the child once again to go more deeply into the history and attempt to establish the details of etiology. The mother related that this family had lived in their own home in a small central Ohio town for the past three years. The house had previously been occupied for a period of ten years by a family whom the mother described as "dirty people." The basement of the house had a dirt floor, and the patient's mother described a peculiar smell that always seemed to be present in the basement. She also said that the patient frequently liked to play in the basement and was often seen putting dirt into her mouth. The dirt floor of the basement was investigated, and numerous samples of dirt from various portions of the floor were taken for microscopic examination. Several of the specimens revealed large numbers of living embryonated ascaris ova (fig. 5). Ova were not found in the feces of the father, mother or one sibling.

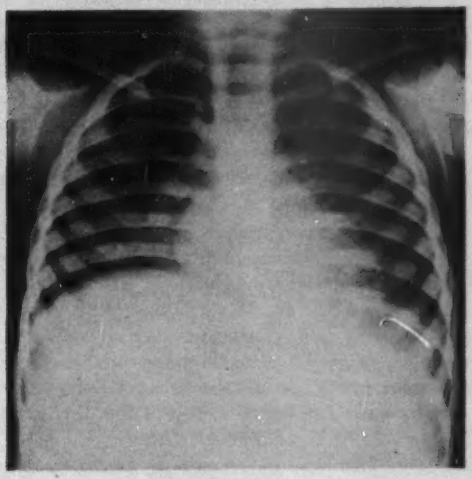

Fig. 4.—Roentgenogram of the chest following therapy with antihistamine agents.

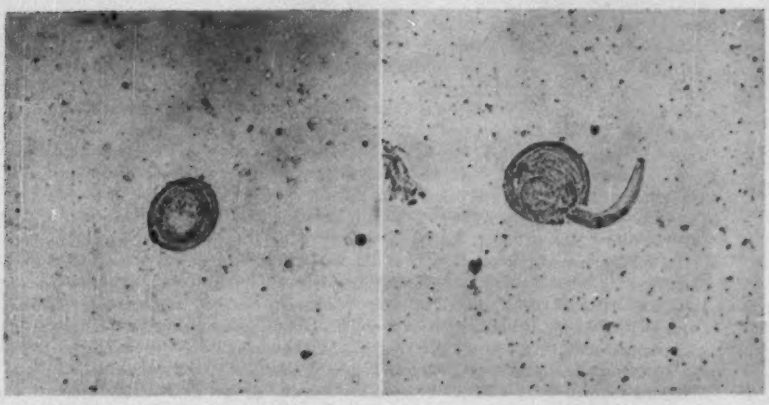

Fig. 5.—Ova recovered from dirt of basement floor. One egg ruptured after being placed under a cover slip. × 120.

COMMENT

With the exception of the hepatomegaly, this case, as well as that of Perlingiero and György and some of those of Zuelzer and Apt, bears a marked resemblance to the described cases of tropical eosinophilia [5] and "chronic" Löffler's syndrome.[6]

Tropical eosinophilia is characterized by severe spasmodic bronchitis, fever, leukocytosis and marked eosinophilia. It differs from Löffler's syndrome in the chronicity of its course, the severity of symptoms and the high degree of eosinophilia, with counts which sometimes reach 80 to 90 per cent.

There is considerable overlapping and confusion in the literature regarding tropical eosinophilia and Löffler's syndrome, and some authors regard them as identical.[7] It would perhaps lead to less confusion to regard them as chronic-severe and transient-mild manifestations of diseases with essentially similar pathogenic bases. As Wise [8] concluded, the two conditions require clinical differentiation because of the morbidity and mortality in the one and the transient character of the other.

Many writers have implicated allergy in the causation of tropical eosinophilia [9] and Löffler's syndrome.[10] Although a great variety of agents have been described in relation to the production of these syndromes,[11] the role played by A. lumbricoides as an etiologic agent is of particular concern to this discussion.

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6. Kartagener, M.: Chronic Eosinophilic Pulmonary Infiltration, Schweiz. med. Wchnschr. **72**:862, 1942.

7. Greig, E. D. W.: Tropical Eosinophilia Associated with Pulmonary Signs (Löffler's Syndrome), J. Trop. Med. **48**:149, 1945-1946.

8. Wise, H. S.: Comparative study of Löffler's and Weingarten's Syndrome, New Orleans M. S. J. **101**:565, 1944.

9. Hodes, P. J., and Wood, F. C.: Eosinophilic Lung (Tropical Eosinophilia), Am. J. M. Sc. **210**:288, 1945. Apley, J., and Grant, G. H.: Tropical Eosinophilia as Seen in England, Lancet **1**:8[illegible]2, 1945.

10. Hansen-Pruss, O. C., and Goodman, E. G.: Allergic Pulmonary Consolidations, Ann. Allergy **2**:85, 1944. Spector, H. I.: Löffler's Syndrome (Transient Pulmonary Infiltrations with Eosinophilia): Report of Case and Review of Available Literature, Dis. of Chest **11**:380, 1945.

11. (*a*) Acarina.—Carter, H. F.; Wedd, G., and D'Abrera, V. St. E.: The Occurrence of Mites (Acarina) in Human Sputum and Their Possible Significance, Indian M. Gaz. **79**:163, 1944. D'Abrera, V. St. E.: Further Observations on Cases of Asthma and Bronchitis Associated with High Eosinophilia and with Mites in Sputum, ibid. **81**:414, 1946. Hall, G. A. M.: Tropical Eosinophilia or Pulmonary Acariasis, Brit. J. Tuberc. **40**:124, 1946. Soysa, E., and Jayawardena, M.: Pulmonary Acariasis: A Possible Cause of Asthma, Brit. M. J. **1**:1, 1945. van der Sar, A.: Pulmonary Acariasis: Relationship to Eosinophil Lung and Löffler's Syndrome, Am. Rev. Tuberc. **53**:440, 1946. Wilson, H. T. H.: Tropical Eosinophilia in East Africa, Brit. M. J. **1**:801, 1947. (*b*) Ankylostoma braziliense.—Wright, D. O., and Gold, E. M.: Löffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis), J. A. M. A. **128**:1082 (Aug. 11) 1945; Löffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis):

It is well known that the larvae of A. lumbricoides in their normal migration from intestine to liver and lung and then back into the intestine usually do not excite conspicuous symptoms. The striking clinical features in this case may be the result of an overwhelming infection, a marked allergic reaction or both. If it is considered that four larvae were found in approximately 1 Gm. of liver, it is obvious that perhaps 1,600 larvae were present in the total mass of the liver. A similar degree of infection may have been present in the lungs.

Müller [12] first suggested that the transitory pulmonary infiltrations of Löffler's syndrome might be due to larval infection of the lungs. He was able to reproduce the lesion in himself by eating soil which was known to be contaminated with animal and human excreta and which

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Report of 26 Cases, Arch. Int. Med. **78**:303 (Sept.) 1946. (*c*) Brucella abortus.—Elsom, K. A., and Ingelfinger, F. J.: Eosinophilia and Pneumonitis in Chronic Brucellosis: Report of 2 Cases, Ann. Int. Med. **16**:995, 1942. (*d*) Coccidioides immitis.—Dickson, E. C.: Coccidioidomycosis: The Preliminary Acute Infection with Fungus Coccidioides, J. A. M. A. **111**:1362 (Oct. 8) 1938. Willett, F. M., and Oppenheim, E.: Pulmonary Infiltrations with Associated Eosinophilia, Am. J. M. Sc. **212**:608, 1946. (*e*) Endomoeba histolytica.—Hoff, A., and Hicks, H. M.: Transient Pulmonary Infiltrations: A Case with Eosinophilia (Löffler's Syndrome) Associated with Amoebiasis, Am. Rev. Tuberc. **45**:194, 1942. Pearlman, A. W.: Löffler's Syndrome, Am. J. Roentgenol. **58**:75, 1947. Randall, T.: Eosinophilic Pneumonitis (Löffler's Syndrome) with Response to Emetine, Brit. J. Tuberc. **39**:37, 1945. Stefano, J.: Asthmatic Syndrome Due to Pulmonary Amebiasis, Semana méd. **2**:749, 1939. (*f*) Fasciola hepatica.—Bernheim, and Jeune: Excessive Eosinophilia: Late Demonstration of Its Parasitic Origin (Hepatic Distomiasis), Lyon méd. **168**:436, 1942. Lavier, G.; Bariéty, M.; Caroli, J., and Boulanger, P.: Hepatic Distomiasis and Löffler Syndrome: Case, Bull. et mém. Soc. méd. d. hôp. de Paris **55**:739, 1939; Paris méd. **1**:434, 1939. (*g*) Mycobacterium tuberculosis.—Leitner, J.: Transient Hyperergic Pulmonary Infiltrations with Eosinophilia in Tuberculosis, Beitr. z. Klin. d. Tuberk. **88**:388, 1936. Leitner, S. J.: Hyperergic, Temporary Infiltration of Lungs Associated with Eosinophilia in Course of Tuberculosis and Abortive Pneumonia, Acta med. Scandinav. **97**:473, 1938. (*h*) Necator americanus.—Venzant Quintana, E.: Löffler Infiltrate Provoked by Necator Americanus, Rev. med.-quir. de Oriente **3**:159, 1942. (*i*) Plant pollens.—Alpher, I. M.: Löffler's Syndrome: Report of Two Cases, One with Recurrent Features and One Associated with Hay Fever, J. Allergy **18**:39, 1947. Engel, D.: Edema Allergicum Vernale: New Disease of Lungs (Popularly Known as Privet Cough), Beitr. z. Klin. d. Tuberk. **87**:239, 1935. Meyer, H. E.: Transitory Pulmonary Infiltrations with Eosinphilia, Med. Welt. **11**:1808, 1937. (*j*) Strongyloides stercoralis.—Berk, J. E.: Transitory Pulmonary Infiltrations, Correspondence, J. A. M. A. **127**:354 (Feb. 10) 1945. (*k*) Sulfonamides.—Ellis, R. V., and McKinlay, C. A.: Allergic Pneumonia, J. Lab. & Clin. Med. **26**:1427, 1941. (*l*) Trichinella spiralis.—Slowey, J. F.: Case of Transient Successive Pulmonary Infiltration, Löffler's Syndrome Associated with Trichiniasis, Ann. Int. Med. **21**:130, 1944.

12. Müller, R. W.: Transitory Pulmonary Infiltrates with Eosinophilia Due to Ascarides in Larval Stage, Beitr. z. Klin. d. Tuberk. **92**:254, 1938; Deutsche med. Wchnschr. **64**:1286, 1938.

may have contained ascaris ova. His work, while widely cited, is highly speculative, for ascaris ova were apparently not looked for in the soil which he consumed.

Koino [13] succeeded in producing a true larval pneumonia in himself by swallowing large quantities of ascaris eggs. He was able to recover larvae in his sputum. However, it is doubtful that this was a true reproduction of Löffler's syndrome, and, as Perlingiero and György pointed out, his experiments did not exactly simulate the natural course of the infection of man by this parasite.

Vogel and Minning,[14] in a well conducted experiment in which adult volunteers swallowed various numbers of ascaris ova, were able to reproduce a disease similar to Löffler's syndrome in every detail. Larvae were not recovered from the sputum in any of their cases.

Although the occurrence of larval pneumonia is mentioned in many of the standard texts [15] and in one [15a] it is stated that "children frequently succumb to pneumonia in this stage of the disease," its occurrence must nevertheless be somewhat rare. No well authenticated case has been described in the past twenty years. Wampler and Sutton,[16] in an extensive study of ascariasis in human beings, were unable to find positive evidence of pulmonary conditions due to the migration of the larva.

Intestinal ascarids have been reported in many cases of Löffler's syndrome,[17] but larvae have never been demonstrated in the liver or in the lungs. It is interesting to note that ascarids were found at autopsy in the intestine in *2* of von Meyenburg's cases.[18]

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13. Koino, cited in Transitory Pulmonary Infiltrations Associated with Eosinophilia—Löffler's Syndrome, editorial, J. A. M. A. **126**:837 (Nov. 25) 1944.

14. Vogel, H., and Minning, W.: Clinical Aspects of Pulmonary Ascariasis and Transitory Eosinophilic Infiltrations, Beitr. z. Klin. d. Tuberk. **98**:620, 1942.

15. (*a*) Ash, J. E., and Spitz, S.: Pathology of Tropical Diseases: an Atlas, Philadelphia, W. B. Saunders Company, 1945. (*b*) Stitt, E. R.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, edited by R. P. Strong, ed. 6, Philadelphia, The Blakiston Company, 1942, vol. 2.

16. Wampler, F. S., and Sutton, L. E., Jr.: Lung Involvement in Human Ascariasis, Virginia M. Monthly **59**:65, 1932.

17. (*a*) Baumann, H.: Eosinophilic Pleurisy with Transitory Eosinophilic Pulmonary Infiltration, Schweiz. med. Wchnschr. **74**:326, 1944. Bertrand-Fontaine, Goutner, and Noufflard, H.: Multinodular Form of Löffler Syndrome Due to Ascaris: Two Cases, Bull. et mém. Soc. méd. d. hôp. de Paris **63**:700, 1947. Froment, R.; Rebatel, and Masson: Löffler Syndrome Due to Ascariasis, Lyon méd. **167**:346, 1942. (*b*) Sommer, E.: Relation Between Ascariasis and Eosinophilic Pulmonary Infiltration, Schweiz. med. Wchnschr. **73**:1132, 1943.

18. (*a*) von Meyenburg, H.: Pathologic Anatomy of "Transitory Pulmonary Infiltrate with Eosinophilia," Virchows Arch. f. path. Anat. **309**:258, 1942. (*b*) von Meyenburg, H.: Eosinophilic Pulmonary Infiltration: Pathology and Pathogenesis, Schweiz. med. Wchnschr. **72**:809, 1942.

In considering the possibility of a hyperergic response, it is well to review the experimental studies of Kerr,[19] who showed that during the initial infection of guinea pigs by Ascaris suis there was only slight tissue response to larvae, whereas repeated infections produced a marked exudative granulomatous response similar to that described in this patient. Biester and Eveleth [20] produced similar lesions in experimental ascariasis of swine. That this response is not specific for ascaris was demonstrated by Taliaferro and Sarles,[21] who produced the identical lesions around the larvae of Nippostrongylus muris in sensitized rats.

It is a well known fact that the ascaris is a powerful antigenic agent. Severe allergic manifestations to it frequently develop in persons who work with this parasite.[22] Campbell has shown that the keratin from A. suis is a powerful eosinophilotactic agent. Zweitel [23] found sensitivity to ascaris extract in 70 per cent of patients with Löffler's syndrome, whereas only 40 per cent of allergic persons and those with known ascariasis reacted to it.

Sommer,[17b] whose reported cases of Löffler's syndrome demonstrated only a single adult male ascaris, pointed out the possible role of sensitivity to ascaris in the production of the syndrome. He contrasted Müller's experiment with that of Koino. Müller, who was sensitized by previous exposure, was able to reproduce the syndrome in himself after the ingestion of what were probably only a few ova. Koino, who was probably not sensitized, did not get a true infiltration after ingesting great quantities of ova.

Sensitivity to ascaris is implicated in our patient by the positive skin response to ascaris extract, the eosinophilia, the hyperglobulinemia and the marked clinical improvement during treatment with antihistamine drugs. Furthermore, our patient had every opportunity to become sensitized to ascaris, since repeated infections were proved by the presence of a large adult worm in the intestine while young and presumably living larvae were present in the liver. It is interesting that

19. Kerr, K. B.: The Cellular Response in Acquired Resistance in Guinea Pigs to an Infestation with Pig Ascaris, Am. J. Hyg. **27**:28, 1930.

20. Biester, H. E., and Eveleth, D. F.: Tissue Studies in Experimental Ascariasis, Am. J. Hyg. **25**:135, 1937.

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22. Manson, P.: Manson's Tropical Diseases: A Manual of Diseases of Warm Climates, edited by P. H. Manson-Bahr, ed. 11, Baltimore, Williams & Wilkins Company, 1940. Campbell, D. H.: Experimental Eosinophilia with Keratin from Ascaris Suum and Other Sources, J. Infect. Dis. **71**:270, 1942.

23. Zweitel, E.: Skin Tests with Ascarides Extract in Transitory Eosinophilic Infiltrates of Lungs, Helvet. med. acta **11**:117, 1944.

the case of the patient of Perlingiero and György is exactly similar, with the exception that larvae were not demonstrated in the liver.

It is noteworthy that repeated examinations of stools since the patient's admission to the hospital have not demonstrated the presence of ova or adult worms, aside from the single adult male observed early in the patient's course. This would imply that the larvae may be trapped or destroyed in the liver and lungs by the hyperergic inflammatory reaction.

From an analysis of our own case as well as those reported in the literature, we suggest that Löffler's syndrome of transient pulmonary infiltrations and eosinophilia may be due in some cases to transient contact of pulmonary tissue with migrating ascaris larvae. That this is not the only etiologic agent is suggested by the large number of cases seen in association with other agents [11] and in particular by the work of Alpher,[11i] who demonstrated the disease after exposure to ragweed pollen. Tropical eosinophilia, with more chronic pulmonary changes, and eosinophilia with visceral manifestations may be due to more prolonged contact with an antigenic stimulus. Such a requirement would be fulfilled in those cases of tropical eosinophilia reported to be associated with mites [11a] in the respiratory tract and in our case, in which the ascaris larvae were trapped by the extensive hyperergic tissue response.

SUMMARY AND CONCLUSIONS

A case is presented in which the syndrome of chronic eosinophilia and eosinophilic granulomatous lesions of the liver has been demonstrated to be caused by the presence within the liver of the larvae of the helminth A. lumbricoides. Pulmonary manifestations are also present and are assumed to be of a similar nature.

Allergy to ascaris is thought to play an important part in the production of this clinical entity. However, the liver does not act as a "shock organ" but, rather, manifests a hyperergic tissue response to the presence of the antigen-producing larvae within it.

This, or a similar mechanism, should be considered when one is investigating the etiologic bases of similar cases.

EFFECT OF HYALURONIDASE ON SKIN REACTIONS TO THE TUBERCULIN PATCH TEST

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NEW YORK

DOES hyaluronidase enhance transepidermal penetration? An answer to this question was sought through experiments with the tuberculin patch test. It was not the primary intention of these experiments to improve the patch test; hyaluronidase is too unstable to be stored in a medium of tuberculin which contains hygroscopic glycerin. However, the answer to the question was of theoretic interest and if positive could find other practical applications.

METHOD

Solutions of hyaluronidase were freshly prepared by injecting 0.5 cc. of isotonic sodium chloride solution into a vial containing 150 turbidity-reducing units of lyophilized hyaluronidase.[1] Of this solution 0.015 cc. was placed on one (marked "H") of the two tuberculin test squares of the tuberculin patch test.[2] The control square of the patch test was prepared with the same amount of hyaluronidase solution in order to rule out the possibility that hyaluronidase itself causes skin reactions. On the second tuberculin test square, 0.015 cc. of isotonic sodium chloride solution was placed. In this way, all three patches of filter paper were moistened with the same amount of fluid, an amount sufficient to moisten them to the edges without leaving any supernatant fluid. This equal amount of moisture in the two tuberculin test squares was a necessary precaution. It eliminated the need for insensible perspiration to dissolve the tuberculin; absorption of tuberculin and skin reaction to tuberculin could start immediately after application of the patch test and simultaneously underneath both tuberculin test squares. Thus, the conditions on the two sides of the tuberculin patch test were identical with the only exception that one tuberculin test square contained hyaluronidase and the other did not. It may be questioned that the two tuberculin test squares of each patch test contained identical amounts of tuberculin. Though quantitative determinations were not done, the process of manufacturing assured equality.

The experiments were carried out on adult volunteers who were known to be positive reactors to tuberculin. The freshly prepared patch tests were applied transversely on the volar surface of the forearm about 1 inch (2.5 cm.) below the cubital fossa. This site of application was chosen to avoid a possible variability of the skin sensitivity, which is said to decrease from the cubital fossa toward the wrist. Volunteers who were known to be highly sensitive to tuberculin removed the patch test after twenty-four hours or earlier and the others after forty-eight hours.

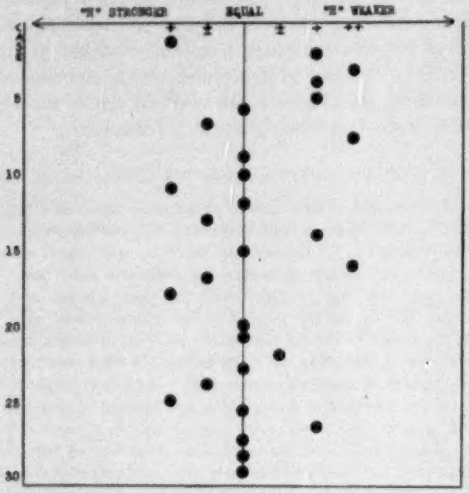
1. Hydase,® Wyeth Incorporated, Philadelphia.

2. The patch tests were supplied by Lederle Laboratories, Division American Cyanamid Company, Pearl River, N. Y.

Excellent cooperation in observing the skin reactions was obtained, since most volunteers were pediatricians or medical students. The entire course of the skin reactions could be followed as to time of onset, extensiveness and intensity of the reactions. I observed the skin reactions at least once and could usually confirm the observations of the volunteers. The areas of skin reactions were measured and their intensity graded from + to 4 +. Differences in either intensity or extensiveness or both were noted as "very slight," (±) "slight" (+) or "moderate" (2 +) and charted accordingly (chart).

RESULTS

The control squares containing hyaluronidase did not elicit any skin reactions.



Skin reactions to the tuberculin patch test, in which one of the tuberculin patches ("H") contains hyaluronidase. The middle line indicates equality of the skin reactions to the two tuberculin patches. The distance from this middle line is the degree of difference between the two reactions.

Of the 30 volunteers, 12 showed equal skin reactions to the two tuberculin test squares, one of which contained hyaluronidase. Nine subjects had a stronger or more widespread skin reaction to the tuberculin test square ("H") containing hyaluronidase. Nine showed a stronger or more extensive reaction to the tuberculin test square which did not contain hyaluronidase. In 3 volunteers the skin reaction appeared somewhat earlier on the "H" side and in 2 on the other side.

In this series, there was no significant difference between the two skin reactions which could be ascribed to the action of hyaluronidase. With the use of the regular tuberculin patch test, the skin reactions

to the two tuberculin test squares frequently differ in size and intensity. This is probably due to many variables but mainly to the degree of firmness with which a tuberculin test square is sealed on the skin by the adhesive. The results of this study were similar to what one would expect from the use of regular tuberculin patch tests not prepared with hyaluronidase.

COMMENT

Hyaluronidase is an enzyme which depolymerizes hyaluronic acid, an acid mucopolysaccharide present in certain mesodermal tissues and acting as a barrier to tissue permeability.[3] This enzymatic action has found practical use in pediatrics [4] mainly to facilitate absorption of fluid given by hypodermoclysis.

The effect of hyaluronidase on the epidermis has not yet been investigated. The results of the present experiments seem to indicate that hyaluronidase has no effect on the epidermis and does not enhance transepidermal penetration.

These negative results may be due to various reasons:

1. *Instability of the Enzyme.*—Testicular hyaluronidase is a labile substance. The claim of the manufacturer that the lyophilized enzyme after solution in isotonic sodium chloride solution is stable at room temperature for two weeks may be too optimistic if the enzyme is exposed on a large surface, as was the case in these experiments. However, only freshly prepared solutions were used and applied to the skin within less than one hour. Whereas heating for thirty minutes at

3. Duran-Reynals, F.: Effect of Extracts of Certain Organs from Normal and Immunized Animals on Infecting Power of Vaccine Virus, J. Exper. Med. **50**:327, 1929; Tissue Permeability and Spreading Factors in Infections: Contribution to the Host-Parasite Problem, Bact. Rev. **6**:197, 1942. McClean, D.: The Influence of Testicular Extracts on Dermal Permeability and the Response of Vaccine Virus, J. Path. & Bact. **33**:1045, 1930; Studies on Diffusing Factors: Methods of Assay of Hyaluronidase and Their Correlation with Skin Diffusing Activity, Biochem. J. **37**:169, 1943. Meyer, K., and Chaffee, E.: The Mucopolysaccharides of Skin, J. Biol. Chem. **138**:491, 1941. McClean, D., and Hale, W. C.: Studies on Diffusing Factors: Hyaluronidase, Activity of Testicular Extract, Bacterial Culture Filtrate and Other Agents That Increase Tissue Permeability, Biochem. J. **35**:159, 1941. Meyer, K.: Biological Significance of Hyaluronic Acid and Hyaluronidase, Physiol. Rev. **27**:335, 1947.

4. Hechter, O.; Dopkeen, S. K., and Yudell, M. H.: Clinical Use of Hyaluronidase in Hypodermoclysis, J. Pediat. **30**:645, 1947. Schwartzman, J.; Henderson, A. T., and King, W. E.: Hyaluronidase in Fluid Administration, ibid. **33**:267, 1948. Schwartzman, J.: Hyaluronidase in Pediatrics, ibid. **34**:559, 1949. Burket, L. C., and György, P.: Clinical Observations on the Use of Hyaluronidase, Pediatrics **3**:56, 1949. Jaworski, A. A., and Farley, J. E., Jr.: Hyaluronidase in the Administration of Fluids, Am. J. Dis. Child. **79**:59 (Jan.) 1950. Schwartzman, J., and Levbarg, M.: Hyaluronidase: Further Evaluation in Pediatrics, J. Pediat. **36**:79, 1950.

65 C. weakens the action of hyaluronidase,[5] skin temperature does not decrease its potency. It is reasonable to assume that under the conditions of these experiments hyaluronidase remained in an active state.

2. *Insufficient Concentration of Hyaluronidase.*—Hyaluronidase is active in minimal amounts. A quantity of 4.5 turbidity-reducing units applied to a skin surface of 1 sq. cm., as used in these experiments, is probably in excess of the required quantity.

3. *Absence of Hyaluronic Acid in the Epidermis.*—Hyaluronic acid is a mesodermal product, whereas the epidermis is an ectodermal structure which is postulated not to contain hyaluronic acid.[6] Though histochemical proof is lacking, this is the most probable reason for the negative results of the present experiments.

4. *Presence of Hyaluronic Acid in the Epidermis in a Chemical State or Linkage Which Is not Acted on by Hyaluronidase.*—This, as well as the presence of a hyaluronidase inhibitor in the epidermis, is a possibility. At present, there is no way to prove or disprove these possibilities. Until more knowledge is available, the absence of hyaluronic acid in the epidermis may be considered as the most acceptable explanation for the failure of hyaluronidase to enhance transepidermal penetration.

SUMMARY

Purified hyaluronidase applied by patch test did not cause any reaction or primary irritation of the skin.

Skin reactions to the tuberculin patch test in tuberculin-sensitive persons were not intensified or accelerated by impregnation of one tuberculin test square with hyaluronidase.

This failure of hyaluronidase to enhance transepidermal penetration is explained by the absence of hyaluronic acid in the epidermis.

25 Central Park West.

Staff members and medical students of Babies Hospital and Vanderbilt Clinic assisted in the experiments.

5. Hobby, G. L.; Dawson, M. H.; Meyer, K., and Chaffee, E.: The Relation Between Spreading Factor and Hyaluronidase, J. Exper. Med. **73**:109, 1941.

6. Meyer, K.: Personal communication to the author.

Case Reports

ERYTHROBLASTOSIS FETALIS IN A SET OF IDENTICAL TWINS

Comparison of Results with Replacement Transfusion and with Conservative Therapy

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The high mortality in erythroblastosis fetalis and the dramatic nature of replacement transfusions have attracted wide attention among both the medical profession and the laity. However, the final value of replacement transfusions has not been completely established. Diamond,[1] in a recent communication, indicated that he was still somewhat hesitant about drawing conclusions from his data, which at that time covered fifteen months of experience and 95 infants personally treated by replacement transfusions. The high death rate before the advent of exchange transfusions (approximately 30 per cent) makes it difficult to deny an erythroblastotic infant a form of therapy claimed to give promising results. On the other hand, it is well known that some infants with this condition and appearing to offer a poor prognosis do recover under what one might term "conservative therapy." The latter comprises repeated small transfusions of suitable Rh-negative blood, in an effort to maintain a red blood cell count of no less than 3,000,000, administration of oxygen and vitamin K and the cautious introduction of feedings. Nevertheless, at present, most workers employ Diamond's criteria[1] for exchange transfusions which are: (1) the demonstration of the presence of antibodies in the mother's circulation; (2) clinical signs of erythroblastosis on the part of the infant—anemia with abnormal numbers of immature red blood cells, jaundice, edema, splenomegaly and hepatomegaly; (3) an Rh-positive infant whose red cells are coated and who has free antibodies in its circulation. A maternal history of previous erythroblastotic infants is also valuable.

Diamond's introduction of the bland polyethylene plastic catheter facilitated the technical side of replacement transfusions. There are three chief routes generally available for this transfusion at present. One is the umbilical vein in the cord stump, which is available for a period of approximately twelve hours following delivery. Recently, transfusions in newborn infants through the abdominal wall segment of the umbilical vein were described by Pinkus.[2] The chief advantage claimed for this method is that it can be used for several days following birth.

From the Departments of Pediatrics and Obstetrics, St. Luke's and Children's Medical Center, and the Division of Pediatrics, Hahnemann Medical College and Hospital of Philadelphia.

1. Diamond, L. K.: Replacement Transfusion as a Treatment for Erythroblastosis Fetalis, Pediatrics **2**:520 (Nov.) 1948.

2. Pinkus, L. R.: Transfusions in Newborn Infants Through Abdominal Wall Segment of Umbilical Vein, J. Pediat. **33**:418 (Oct.) 1948.

Arnold and Alford [3] described the use of the great saphenous vein for replacement transfusions. This vein has the advantage of being definitely available when the umbilical vein is no longer patent. However, the value of replacement transfusion rests to a large extent on its being carried out within the first twenty-four hours after delivery.

The opportunity to treat a set of identical twins with erythroblastosis fetalis of the icterus gravis type is an infrequent one. The more seriously affected of these twins received an exchange transfusion, while the other one was treated by the "conservative" approach. It is felt that this feature is unique and justifies this report.

REPORT OF A CASE

On Sept. 7, 1948, a 25 year old white woman, unipara, secundigravida, was admitted to the obstetric service of one of us (L. K.) at St. Luke's and Children's Medical Center. The one previous pregnancy terminated in a live birth. The mother had been under an obstetrician's care for both pregnancies and on each occasion had had Rh factor determinations done. She was reported as being Rh positive. She had a normal spontaneous delivery of identical male twins, A weighing 6 pounds 9 ounces (2,977 Gm.) and B weighing 7 pounds (3,175 Gm.) at birth. Resuscitation was uneventful, and both infants received routine immediate neonatal care and were transferred to the nursery in apparently good condition.

In both infants, jaundice was first reported twelve hours after delivery. The patients were first seen by one of us (R. S. W.) at 16 hours of age, at which time both infants were clinically jaundiced. Twin A appeared the more icteric of the 2 and had a definitely palpable liver and spleen, these being about 2 cm. below the costal margin. Twin B was seriously jaundiced, but perhaps less so than his brother. At this time, his liver and spleen were not enlarged on clinical examination. Despite the history of the mother's being Rh positive, erythroblastosis was considered. Blood typing of both infants was done, as well as a complete blood count. Both infants belonged to group A and were found to be Rh positive. The mother's typing was repeated at the hospital, and she was found to be group A, Rh negative. Infant A had a red blood cell count of 3,800,000, with 79 per cent hemoglobin. The differential count revealed 62 nucleated red blood cells per 100 white cells counted. The white blood cell count was 25,400. Twin B had a red blood cell count of 4,200,000, a hemoglobin concentration of 84 per cent and 10 nucleated red cells per 100 white blood cells, with a leukocyte count of 24,500. It was decided to give twin A an exchange transfusion and to use twin B as somewhat of a control.

The technic of the exchange transfusion was essentially that described by Arnold and Alford,[3] with the use of the great saphenous vein just distal to its junction with the femoral vein and the introduction of a polyethylene catheter, 18 gage, up into the inferior vena cava. The use of two 20 cc. syringes alternating withdrawal and replacement of 20 cc. quantities of blood seemed to eliminate the clotting tendency to a greater degree than the technic employing the three way stopcocks. It was not necessary to inject heparin through the apparatus. Four hundred and fifty cubic centimeters of the infant's blood was removed, and 495 cc. of blood was given. The replacement was completed in two hours and was terminated by the intravenous injection of 10 cc. of 5 per cent solution of calcium gluconate U. S. P. The infant withstood the procedure reasonably well, having

3. Arnold, D. P., and Alford, K. M.: A New Technique for Replacement Transfusion in the Treatment of Hemolytic Disease of the Newborn Infant, J. Pediat. **32**:113 (Feb.) 1948.

received oxygen and external application of heat continuously during the procedure. He was then placed in an incubator with further continuous administration of oxygen. He also received penicillin on a prophylactic basis, 10,000 units every three hours for forty-eight hours. Figures 1 and 2 will help to clarify the subsequent course of both these infants. It was necessary for twin A to receive two small transfusions subsequent to the exchange transfusion because of a fall in the red blood cell count below the desired level. These were given on the sixth and ninth days of life, the quantity being 60 cc. on each occasion. Twin B, without an exchange transfusion, maintained a red blood cell count in the vicinity of 4,000,000 until the fifth day, when a sudden drop to 1,900,000 was observed. He received at once 75 cc. of blood and on the sixth and ninth days 60 and 35 cc., respectively. The jaundice, splenomegaly and hepatomegaly receded rapidly in twin A, whereas in twin B the jaundice persisted for about four weeks after birth. Twin A, at the time of his discharge from the hospital on the thirteenth day, was clinically free from jaundice. Twin A had regained his weight at birth at 10 days of age, whereas twin B was 5 ounces (142 Gm.) below his weight at birth on the seventeenth day, the time of his discharge. Twin B gained more slowly. Twin A had a generalized convulsion and several episodes of twitching about twelve hours after the exchange transfusion was completed. A lumbar puncture done at that time revealed yellow spinal fluid. Phenobarbital sodium was given on four occasions; the twitching ceased, and the infant then made a rapid recovery.

At 9 months of age both twins appeared to be developing normally. However, twin B, the one receiving the "conservative therapy," was somewhat more advanced in motor development. He attempted to walk with support, whereas the other twin sat up by himself but was not interested in standing or walking. The residual anemia was gradually overcome by means of diet and iron therapy. At 5 months of age, both red blood cell counts were over 4,000,000 and the hemoglobin concentration was approximately 10 Gm. for each infant.

COMMENT

Unfortunately, a blood specimen for antibody titer was not taken from twin A prior to the exchange transfusion. At the end of the transfusion, his blood was Rh negative and did not reveal any anti-Rh agglutinins. This, of course, showed the effect of the exchange transfusion. In order to ascertain the exact status of the blood typing of the mother and the infants, complete typing was repeated at the Philadelphia Serum Exchange. On May 27, 1949, the twins were found to be group A, Rh_1Rh_0.[4] At birth twin B had been shown to be group A and weakly Rh positive, and, while there was a weak trace of antibody activity in the serum, it was found only in the undiluted specimen. The mother was found to be group A, Rh" and had anti-Rh_0 agglutinins, the titer being 1:32 in albumin and 1:32 in saline solution. It is interesting to note that technically, then, both the infants and the mother were Rh positive, except that the infants possessed all three Rh antigens, whereas the mother possessed only the Rh" antigen.[4] Consequently, the mother's blood was stimulated to produce anti-Rh_0 agglutinins. Therefore, for all practical purposes, she behaved as though she were Rh negative. The blood of the first-born child, now 2½ years old, was typed and found to be group O, Rh, Rh_0.

4. Wiener, A. S.: The Rh Blood Types and Some of Their Applications, Am. J. Clin. Path. **15**:106 (March) 1945.

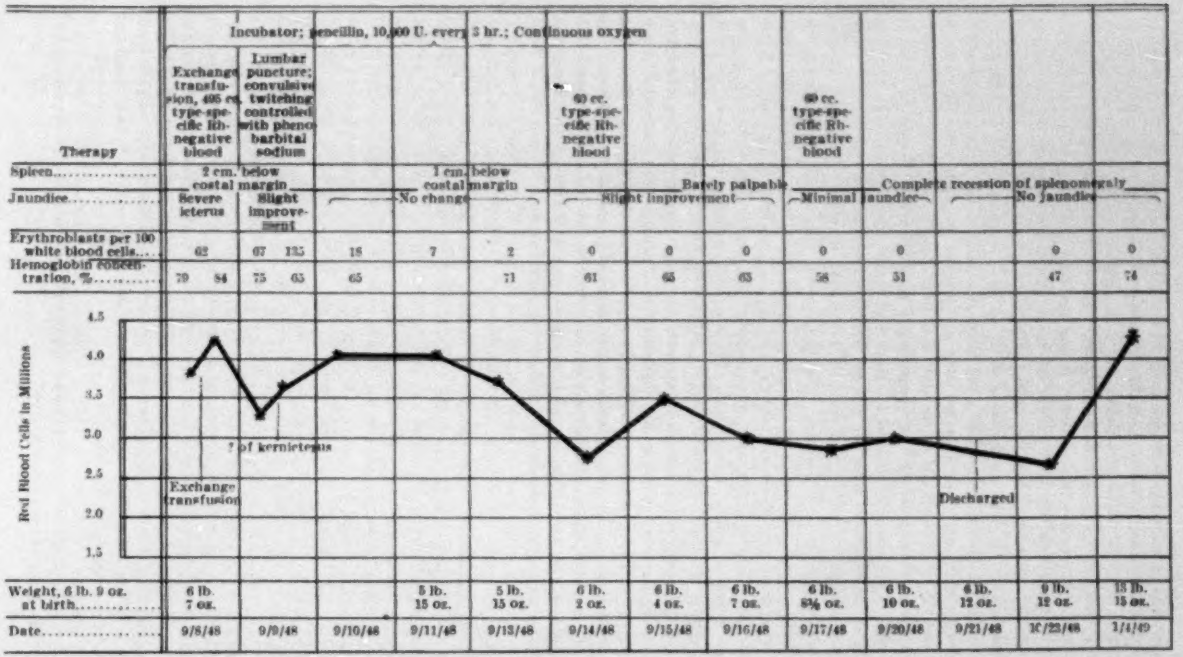

Fig. 1.—Graphic representation of clinical course of twin A following exchangetransfusion.

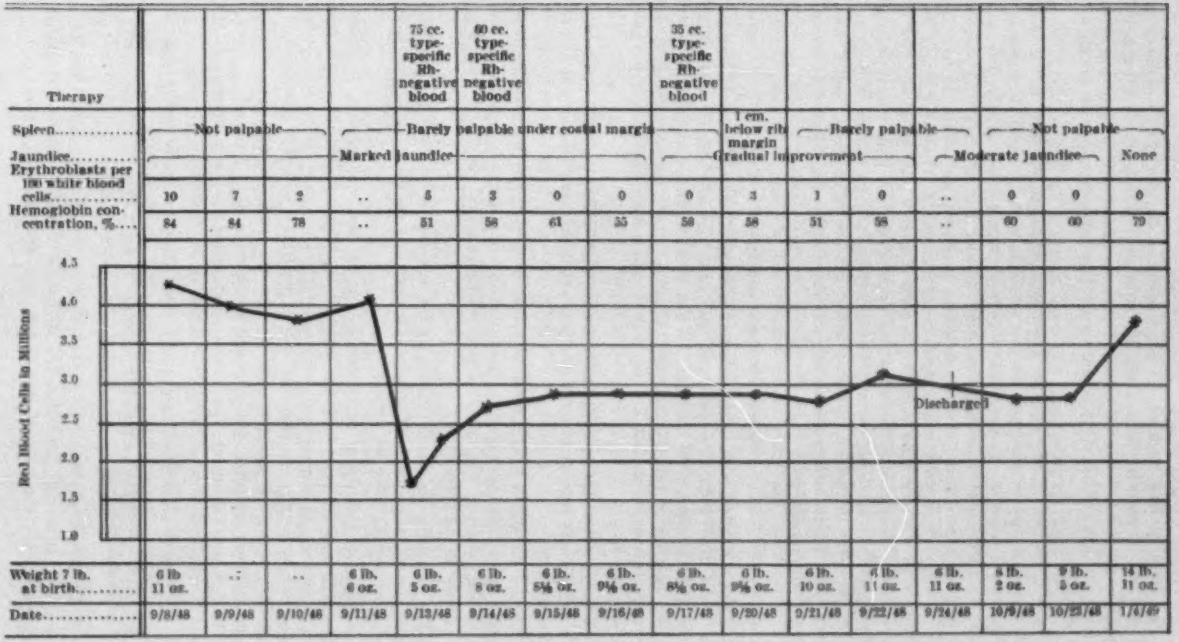

Fig. 2.—Graphic representation of clinical course of twin B in response to "conservative therapy."

In a study in New York city of 645 Caucasians, Rh type, Rh" was found in 0.5 per cent of them by Wiener and his associates.[5] The mother's Rh-negative typing in the hospital was, of course, due to the fact that the typing was done with an anti-Rh$_0$ (85 per cent) typing serum. This indicates one of the limitations of this method.

It is interesting to note that the exchange transfusion was used on the twin who offered the poorer prognosis and that following the transfusion the immediate course was a smoother one than that of the twin treated conservatively. This was shown by a more rapidly fading jaundice and a better gain in weight. As regards the ultimate picture, there was little difference between these infants. In fact, the one treated conservatively was somewhat more advanced. Clinically, it was the feeling of all who saw these patients that twin A gave a poor prognosis prior to the exchange transfusion. The infant was cyanotic and apathetic, had a palpable spleen and liver, was jaundiced and anemic and had a large number of immature red blood cells. In contrast, the other infant had less splenomegaly and a much better blood picture, was not cyanotic, was more active and, in general, offered a better appearance.

SUMMARY AND CONCLUSION

A set of identical male twins with erythroblastosis fetalis was treated twenty-four hours after birth. The twin who was more seriously affected received an exchange transfusion, while the other one was given "conservative therapy." Both infants went on to complete recovery. However, the infant who received the exchange transfusion showed a more prompt return to normal, despite his poor initial prognosis.

A nine month follow-up examination showed both infants progressing normally, although the less severely affected twin was somewhat more advanced as regards motor activity.

Despite the unique opportunities presented by a set of erythroblastotic twins treated by two methods, no final conclusion can be drawn. It was the general impression, however, that the child given exchange transfusion had a poor prognosis prior to this therapy.

The hemolytic anemia was based on the development of anti-Rh agglutinins by the mother, who, while Rh positive, possessed only the Rh antigen. The twins both possessed all three Rh factors.

ADDENDUM.—Subsequent experience during the past year appears to demonstrate further the value of exchange transfusions. The umbilical vein in the cord can be used for at least twenty-four hours in many cases. The umbilical route seems preferable over the saphenous vein route from a technical standpoint.

Rapid clearing of jaundice appears to be the usual experience in erythroblastotic infants who have had an exchange transfusion.

Twin A now exhibits slight weakness of left upper and lower extremities. His development is about two months behind that of his brother.

1111 North Sixty-Third Street (31) (Dr. Agerty).

Dr. Neva Abelson, of the Philadelphia Serum Exchange, did the blood typing and advised in this case.

5. Wiener, A. S.; Sonn, E. B., and Polivka, H. R.: Heredity of Rh Blood Types: V. Improved Nomenclature; Additional Family Studies with Special Reference to Hr, Proc. Soc. Exper. Biol. & Med. **61**:382 (April) 1946.

COEXISTENCE OF DIABETES INSIPIDUS AND DIABETES MELLITUS IN A SEVEN YEAR OLD GIRL

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The occurrence of diabetes mellitus and diabetes insipidus in the same patient is rare. Greene and Gibson[1] reviewed the literature to 1939 and found a total of 20 cases. As these authors pointed out, however, the diagnosis in many of these is questionable, owing to inadequate laboratory studies. They described an additional case of their own. Since that time, 6 more cases have been reported in the available literature.[2] Of the 27 cases, only 2 have been of patients within the pediatric age group: a 13 year old boy studied by Mouriquand, Dauvergne and Monnet[2d] and a 14 year old boy reported on by Allan and Rowntree.[3] The possibility that a single lesion may cause both diseases or that their association is purely coincidental has been discussed in several of the reports. The present case is of interest because of the uncommonness of the condition and because it is of the youngest patient to be recorded. Both the other children reported on manifested disturbances of growth and development, i. e., infantilism, while our patient displayed no similar changes.

REPORT OF CASE

M. C. was first admitted to the University Hospital on May 19, 1945, at the age of 7 years 6 months. The chief complaint given by the parents was that she "drank too much water." The exact time of onset of the present illness could not be ascertained from the history, but her mother and father were aware that she

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From the Diabetic Clinic of the Department of Pediatrics and Communicable Diseases, University Hospital.

1. Greene, J. A., and Gibson, R. B.: Coexistence of Diabetes Mellitus and Diabetes Insipidus: Report of a Case with Pregnancy, J. Lab. & Clin. Med. **24**: 455-457 (Jan.) 1939.

2. (*a*) Gray, P. A., and Moffat, W. M.: Coexistence of Diabetes Mellitus and Diabetes Insipidus: Case Report with Autopsy, Endocrinology **27**:430-433 (Sept.) 1940. (*b*) McPherson, E.: Case of Diabetes Mellitus, Associated with Lesions of Pituitary Body, Glasgow M. J. **131**:220-224 (May) 1939. (*c*) Moloney, G. E.: Diabetes Mellitus Associated with Diabetes Insipidus, New Zealand M. J. **38**:263-266 (Aug.) 1939. (*d*) Mouriquand, G.; Dauvergne, M., and Monnet, P.: Coexistence de diabète inspide, diabète sucré et infantilisme chez un enfant de 13 ans, Lyon méd. **168**:438-449 (Dec. 6) 1942. (*e*) Rutledge, D. I., and Rynerson, E. H.: Diabetes Insipidus: I. Coexistence of Diabetes Mellitus and Diabetes Insipidus, Proc. Staff Meet., Mayo Clin. **14**:441-443 (July) 1939. (*f*) Talbott, J. H.; Coombs, F. S.; Consolazio, W. V., and Pecora, L. J.: Diabetes Insipidus Associated with Diabetes Mellitus: Metabolic Studies and Report of a Case, Arch. Int. Med. **66**:607-624 (Sept.) 1940.

3. Allan, F. N., and Rowntree, L. G.: The Association of Diabetes Insipidus and Diabetes Mellitus, Endocrinology **15**:97-106 (March-April) 1931.

had "always" drunk large quantities of water and passed large amounts of urine at frequent intervals. Three months prior to her admission to this hospital it was noted that the girl had lost weight and she was taken to her family physician. A diagnosis of diabetes mellitus was made as a result of his examination, and the patient was given 20 units of insulin injection U. S. P. twice each day until her admission to this hospital. During this three month interval she experienced numerous episodes of weakness, hunger, faintness and, on at least two occasions, loss of consciousness for brief periods. One of these attacks was also accompanied with a mild generalized clonic convulsion.

The patient was the product of a full term, uncomplicated pregnancy and weighed between 8 and 9 pounds (3,629 and 4,082 Gm.) at birth. The developmental history was incomplete, but her parents stated she said words at 1 year of age and began to walk at the same time. She had always been healthy until the onset of the present illness except for mild and uncomplicated chickenpox and measles.

Both parents were living and well. It was the impression of the interrogator that the parents were below average intelligence and that any history obtained from them was not completely reliable. The patient was the second of four children. The oldest died at the age of 9 years from an unknown cause. Another child died at 4 years of age in coma from a condition presumed to have been diabetes mellitus. This diagnosis was made terminally by a local physician. The third child died twenty-four hours after birth. Permission for autopsy was not obtained. No further family history was available.

At the time of her admission, the patient did not appear acutely or chronically ill. Her height was 44½ inches (113 cm.) and her weight was 50 pounds (22.7 Kg.). Temperature, pulse rate and respirations were normal. The blood pressure was 100 systolic and 50 diastolic. Her sensorium was clear, but her reply to questions gave the impression of mild mental retardation. There were no abnormal neurologic signs and the results of the remainder of her physical examination were in no way remarkable.

Routine laboratory studies revealed normal red and white blood cell counts, a negative Kahn reaction and a negative reaction to the tuberculin test (1:1,000 old tuberculin). The urine had a specific gravity of 1.003 and contained a trace of sugar and acetone and diacetic acid. Otherwise, the urinalysis revealed nothing abnormal.

During the first few days in the hospital she had an insatiable thirst and her urinary output for any twenty-four hour period varied between 7,000 and 10,000 cc., with a specific gravity that never exceeded 1.003. Except for that detected on the initial urinalysis, glycosuria and ketonuria were absent, despite the fact that the patient was receiving no insulin and was on a routine diet. It was felt that the diagnosis of diabetes mellitus might be an error and that she had, instead, diabetes insipidus.

With the latter diagnosis in mind, a urine concentration test was carried out. During a twelve hour period the specific gravity of the urine never exceeded 1.004. The patient was then given 1 cc. of beta-hypophamine (pitressin®) tannate N. N. R. daily. This caused the polyuria to become greatly diminished and the concentration of the urine increased. Simultaneously, glycosuria again was present in nearly all specimens of urine and ketonuria was occasionally found also. At that time a fasting blood sugar level was 228 mg. per hundred cubic centimeters. The administration of beta-hypophamine tannate was stopped. A dextrose tolerance test

was then performed, with the results shown in the tabulation. The patient was given a preparatory diet for three days preceding this test. The amount of dextrose ingested was 1.75 Gm. per kilogram of body weight.

Time, Hours	Blood Sugar (Capillary) Mg./100 Cc.	Presence of Sugar in Urine
Fasting	719	0
1	517	+++
1½	517	++++
2	418	++++
3	332	+++
4	214	0
5	169	0

Following control of the diabetes mellitus with the use of insulin, an eighteen hour concentration of urine gave a specific gravity of 1.008. Because of evidence of severe dehydration and weakness in the patient after this interval, any attempt at a longer period of concentration had to be abandoned. The patient was carefully observed throughout the duration of the test period as she made many attempts to obtain fluid.

To rule out the possibility of a renal defect accounting for the inability to concentrate urine, the following studies were carried out with the results noted: A phenolsulfonphthalein test showed excretion of 77 per cent of the dye in thirty minutes and of 82 per cent at the end of one hour. Values for blood nonprotein nitrogen varied from 14 to 24 mg. per hundred cubic centimeters on several occasions. The appearance on retrograde pyelograms was entirely normal.

Additional diagnostic procedures were completed to exclude possible causes of diabetes insipidus. Roentgenograms of the skull, long bones, pelvis and chest showed no abnormalities. A pneumoencephalogram was interpreted as being normal. Examination of the spinal fluid revealed normal dynamics of pressure, no cells and a quantitative protein measurement of 22 mg. per hundred cubic centimeters. The reaction to a Kahn test on the spinal fluid was reported as negative. A funduscopic examination also showed a normal condition. Psychometric examinations revealed an intelligence quotient of 70 and were considered a reliable index of her mental status.

While she was in the hospital, the diabetes mellitus was controlled with the use of insulin injection and diet. At the time of her discharge from the hospital she was on a regimen of 12 units of insulin before breakfast, 6 units before lunch and 5 units before supper. Her diet consisted of a total of 1,700 calories, 20 per cent protein and 40 per cent carbohydrate. This program kept her relatively aglycosuric and resulted in normal fasting blood sugar levels. The diabetes insipidus was treated with 1 cc. of beta-hypophamine tannate in oil hypodermically daily. While she received this medication, her abnormal thirst subsided, the polyuria decreased and the specific gravity of the urine reached values of 1.020.

This girl has been followed at regular intervals since her first admission. In March 1947, at the age of 9 years, she was brought into the hospital for reevaluation of her condition. At that time, her height was 48 inches (122 cm.) and her weight was 57 pounds (25.9 Kg.). Her blood pressure was 100 systolic and 60 diastolic. The results of physical examination were not remarkable.

Four days after withdrawal of the beta-hypophamine tannate a urine concentration test over twelve hours gave a specific gravity of 1.003. At the same time the extreme thirst returned. Routine urinalyses otherwise gave entirely normal results except for occasional traces of sugar. Roentgenologic examinations of the skull and long bones again revealed no abnormality. Repeated blood Kahn and tuberculin

tests gave negative reactions. Determinations showed the blood nonprotein nitrogen to be 17 mg. and the total blood protein, 7.0 Gm. per hundred cubic centimeters; chloride was 106 milliequivalents, bicarbonate, 25 milliequivalents and total base, 155 milliequivalents, per liter. A twenty-four hour specimen of urine had normal levels of the 17-ketosteroids and follicular stimulating hormones for a child of her age. An electroencephalogram was obtained and the tracings were read as being abnormal and consistent with diffuse generalized changes in the brain, probably of a degenerative nature. Attempts at localization of a lesion were unsuccessful. A complete ocular examination, including measurement of visual fields, revealed no abnormalities. A psychometric study gave her an intelligence quotient of 74, agreeing with the previous results.

In July 1948 (at the age of 10 years 8 months), M. C. was 50½ inches (128 cm.) tall and weighed 70 pounds (31.8 Kg.). A complete physical examination showed no abnormalities. A fasting blood sugar level was 113 mg. per hundred cubic centimeters. Urinalysis revealed no new findings. Her dosage of insulin had been gradually increased, and she received 22 units of protamine zinc-insulin injection U. S. P. and 11 units of insulin injection U. S. P. in separate syringes before breakfast. She was maintained on the same dosage of 1 cc. of beta-hypophamine tannate daily.

COMMENT

All the criteria for a diagnosis of both diabetes mellitus and diabetes insipidus were satisfied in this girl. She had glycosuria, hyperglycemia and ketonuria which responded to insulin therapy. The glycosuria was inconstant initially because of the extreme dilution of the urine as a consequence of the associated diabetes insipidus, but concentration of the urine with beta-hypophamine tannate resulted in its reappearance. She had a diagnostic blood sugar level on fasting, and a typical diabetic curve for dextrose tolerance. The presence of diabetes mellitus, therefore, seems established. The intense thirst and the pronounced polyuria are characteristic of diabetes insipidus and continued after control of the diabetes mellitus. The low specific gravity of the urine following an attempt at its concentration is further evidence. Finally, the remarkable response of the polydipsia and polyuria to specific therapy with extract of the posterior lobe of the pituitary gland confirms the diagnosis. It is felt that other possible causes of polyuria, such as emotional factors and renal abnormalities, were excluded.

In a consideration of the differential diagnosis, Lewin,[4] Talbott and his associates[2f] and others[5] pointed out that transient glycosuria can occur in diabetes insipidus. Intracranial injury may produce transient glycosuria and a transient or permanent polyuria.[6] It is quite possible that some of the earlier reported cases of associated diabetes mellitus and diabetes insipidus might have fallen into one of these categories. The development of better technics in studying metabolic disorders and the introduction of specific therapeutic agents have greatly facilitated the confirmation of such a diagnosis, as exemplified in our case. The failure to

4. Lewin, C.: Zur Frage des Zusammenhangs des Diabetes mellitus und Diabetes insipidus, Med. Klin. **15**:133-136 (Feb. 6) 1919.

5. (*a*) Allan and Rowntree.[2] (*b*) Duncan, G. G.: Diseases of Metabolism: Detailed Methods of Diagnosis and Treatment; A Text for the Practitioner, ed. 2, Philadelphia, W. B. Saunders Company, 1947, pp. 746-747.

6. (**a**) Lewin.[4] (*b*) Duncan.[5b] (*c*) Warkany, J., and Mitchell, A. G.: Diabetes Insipidus in Children: A Critical Review of Etiology, Diagnosis and Treatment, with Report of Four Cases, Am. J. Dis. Child. **57**:603-666 (March) 1939.

demonstrate a consistent glycosuria until the use of beta-hypophamine tannate, which caused a concentration of urine of sufficient degree to show the presence of sugar, is of importance. When one suspects the coexistence of the two diseases, this possibility must be recognized.

Whether both diseases in the patient under discussion may have a common or related origin is an interesting point for speculation and involves a consideration of the possible etiologic bases of the two conditions. The pathogenesis of diabetes mellitus remains obscure. It has been known for many years that removal of the pancreas from an animal produces a syndrome resembling diabetes mellitus.[7] However, the anatomic studies of the pancreas which have been observed at necropsies in patients with clinical evidence of the disease have been disappointing in that specific lesions are frequently absent.[8] The work of Houssay[9] and Long,[10] showing the relationship of the anterior lobe of the hypophysis to diabetes mellitus and, particularly, the fact that injection of extract from the pituitary can produce permanent glycosuria and hyperglycemia, has reopened the entire question of the causation of the disease.[11]

The relationship of the central nervous system to carbohydrate metabolism is not well understood at present.[12] Claude Bernard was able to produce a temporary hyperglycemia and glycosuria in animals by injury to the floor of the fourth ventricle.[12c] Experimental lesions in the posterior part of the hypothalamus have produced similar changes, apparently through stimulation of the adrenal glands and depletion of hepatic glycogen. However, none of these conditions can be strictly compared with the clinical picture of diabetes mellitus.

Warkany and Mitchell[6c] reviewed the possible causes producing the symptom complex of diabetes insipidus in children. They concluded that the lesion must involve one or more of the following structures: the nucleus supraopticus in the hypothalamus, the supraopticohypothalamic tract or the pars nervosa (posterior lobe of the pituitary). Complete destruction of the pituitary body will not cause polyuria and polydipsia, as the anterior part of the hypophysis must remain intact for the syndrome of diabetes insipidus to occur.[13] It is felt that the following possible causes of the condition in our patient were ruled out: cerebral trauma, encephalitis, tuberculosis, syphilis, xanthomatosis and tumor. The abnormal electroencephalogram suggests some degenerative process which has made no apparent progress in the three and a half years that the patient was followed.

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7. (*a*) Baily, C. C., and Baily, O. T.: Alloxan Diabetes, Proc. Am. Diabetes. A. **6**:373-387, 1946. (*b*) Warrens, S.: The Pathology of Diabetes Mellitus, ed. 2, Philadelphia, Lea & Febiger, 1938.

8. (*a*) Warren.[7b] (*b*) Joslin, E. P.; Root, H. F.; White, P.; Marble, A. M., and Baily, C. C.: The Treatment of Diabetes Mellitus, ed. 8, Philadelphia, Lea & Febiger, 1946. (*c*) MacCallum, W. G.: A Textbook of Pathology, ed. 7, Philadelphia, W. B. Saunders Company, 1940, p. 956.

9. Houssay, B. A.: Carbohydrate Metabolism, New England J. Med. **214**: 971-982 (May) 1936.

10. Long, C. N. H.: The Influence of the Pituitary and Adrenal Glands upon Pancreatic Diabetes, Medicine **16**:215-247 (Sept.) 1937.

11. Young, F. G.: Experimental Investigations on Relations of Anterior Hypophysis to Diabetes Mellitus, Proc. Roy. Soc. Med. **31**:1305-1316, 1938.

12. (*a*) Duncan.[8b] (*b*) Joslin and others.[8b] (*c*) Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 3, Baltimore, Williams & Wilkins Company, 1943, pp. 992 and 993.

13. Warkany and Mitchell.[6c] Best and Taylor.[12c]

Consideration of these facts reveals that the hypophysis and closely related cerebral structures may play a major role in the origins of diabetes insipidus and diabetes mellitus. There is strong evidence that our patient had a widespread neurologic lesion which could conceivably have affected the pertinent structures, leading to the double syndrome. However, there was no evidence of pituitary dyscrasia other than the diabetes mellitus and diabetes insipidus. There were no abnormalities of growth in stature or weight. Bone maturation was consistent with age, and the urinary excretion of 17-ketosteroids and follicular stimulating hormones was normal. Repeated roentgenograms of the skull, a pneumoencephalogram and ocular examinations failed to suggest involvement of the pituitary. The possibility that a common lesion was responsible for both forms of diabetes in this girl, therefore, remains hypothetic.

One of the patients described by Allan and Rowntree [3] and the one presented by Mouriquand and his co-workers [2d] had dwarfism and infantilism, conditions which are most frequently associated with hypophysial or hypothalamic lesions.[14] In neither patient was a definite causation established. Talbott and his associates [2f] speculated that a common cause was the explanation for the symptoms in their patient. They pointed out that the occurrence of diabetes mellitus may be associated with pituitary tumors, as in Cushing's syndrome (pituitary basophilism). However, there is no proof that Cushing's syndrome is caused by an overproduction of pituitary hormones and the primary lesion is more apt to involve the adrenal cortex.[15] Gray and Moffat [2a] were unable to observe evidence at necropsy in their patient that a single lesion was responsible for both diabetes insipidus and diabetes mellitus. The pathologic report by McPherson [2b] was equivocal. Others [16] concluded that the relation of the two diseases remains obscure and that their association may be no greater than would result from pure coincidence.

SUMMARY

The coexistence of diabetes mellitus and diabetis insipidus is uncommon. A case is described of a 7 year old girl in whom both diagnoses were substantiated. Her condition responded satisfactorily to treatment with diet, insulin injection and extract of the posterior lobe of the pituitary. The pathogenesis of the two diseases is discussed, and the possible relationship of both to a single lesion is postulated but remains unproved in the case presented.

University Hospital.

14. Grollman, A.: Essentials of Endocrinology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947, pp. 128-130. Selye, H.: Textbook of Endocrinology, Montreal, Acta Endocrinol. Univ. de Montreal, 1947, p. 299.

15. Footnote 14. Albright, F.: Cushing's Syndrome: Its Pathological Physiology, Its Relationship to Adreno-Genital Syndrome, and Its Connection with the Problem of Reaction of Body to Injurious Agents ("Alarm Reaction" of Selye), in Harvey Lectures, 1942-1943, Baltimore, Williams & Wilkins Company, 1943, pp. 123-140.

16. Greene and Gibson.[1] Young.[11] Lawrence, R. D., and McCance, R. A.: Diabetes Mellitus and Insipidus Associated in One Case, Lancet **1**:76-77 (Jan.) 1933.

RETROPERITONEAL TERATOMA IN INFANCY

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Retroperitoneal teratomas in infancy are exceedingly rare. In 1943, Arnheim [1] reported a case with recovery, that of a 3 month old infant, and he reviewed the literature. He collected 23 additional reported cases; 19 of them were of children under 2 years of age. Progressive enlargement of the abdomen and the presence of an intra-abdominal mass were the salient clinical diagnostic features. Of the 24 cases, 12 were observed at autopsy and 12 at operation. Only 4 infants survived the operation and were cured. The following presentation is the fifth reported of recovery.

REPORT OF A CASE

History.—A female infant 3 months of age was admitted to the Lebanon Hospital on Jan. 19, 1948. The infant was born at full term, weighing 7 pounds 5 ounces (3,317 Gm.). Delivery was spontaneous. At 2 months of age, it was first noted that the child's abdomen was unusually large, but the child was comfortable, ate well and gained weight. At 3 months of age, the abdomen was larger, and the child was uncomfortable lying prone.

Physical Examination.—The infant was well developed and well nourished, weighing 14 pounds (6,350 Gm.). Results of physical examination, except for those referable to the abdomen, were normal. The abdomen was much enlarged; the flanks bulged, there being a little more fulness on the right side than on the left. On palpation, a large, firm, irregular mass was felt, filling the upper two thirds of the right side of the abdomen and extending past the midline to the left upper quadrant. The outlines of this mass differed at each subsequent examination. This area was dull to percussion. The spleen was not palpable. Rectal examination showed nothing abnormal.

Laboratory Data.—The urine and the peripheral blood did not show any abnormalities. Blood sugar measured 80 mg., urea nitrogen 13 mg. and cholesterol 150 mg., per hundred cubic centimeters.

Roentgenologic examination of the abdomen disclosed a large mass containing numerous calcified areas. This mass appeared to the right and to the left of the midline and somewhat posterior. It was the impression of the roentgenologist that the mass was a teratoma.

Operation.—After a transfusion of 90 cc. of blood, the operation was performed by one of us (B. S.). With the patient under anesthesia induced by ether, a long right rectus incision was made. On opening the peritoneum, a large, retroperitoneal, multiloculated, cystic mass, about 6 inches (15 cm.) in diameter, was seen, pushing the right kidney caudally and the right lobe of the liver upward.

From the Pediatric and Surgical Services of Lebanon Hospital.

1. Arnheim, E. E.: J. Mt. Sinai Hosp. **10**:355 (July) 1943.

Fig. 1.—Lateral roentgenogram demonstrating calcified tumor mass.

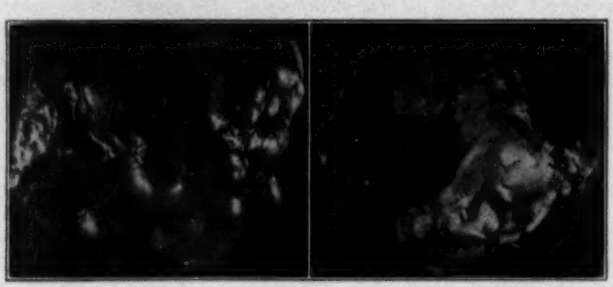

Fig. 2.—Photographs of gross specimen. Left view is of the external surface showing general configuration, nodular character and cysts. Right view shows cut surface with large emptied cyst to left. Irregular parenchymatous, grayish tissue is on the right. Sections of this tissue disclosed various organoids described in text.

The ascending and transverse portions of the colon were displaced to the left and anteriorly. The lateral peritoneal fold of the ascending colon was incised. The tumor was enucleated by blunt dissection. It apparently arose from an area immediately above the right kidney. The pedicle of the tumor mass contained several blood vessels which were ligated and cut. It was felt that the circulation to the right kidney was impaired, and a nephrectomy was performed. There were several small glands present in the retroperitoneal space. The abdominal wall was closed in layers.

Fig. 3.—Photomicrograph showing fully developed large intestinal tissue. Note mucosa, muscularis mucosae, submucosa, longitudinal and circular muscularis, adipose tissue, serosa, vessels and nerves; × 60.

Course in the Hospital.—The patient withstood the operation well. One hundred cubic centimeters of blood was given after the operation. Fluids were supplied parenterally twice daily for four days. Penicillin, 80,000 units, was given intramuscularly daily. Feedings were started on the day after the operation. The temperature was normal within thirty-six hours. The patient was discharged from the hospital in excellent condition on the ninth postoperative day. One year

after the operation the child is doing well, has remained in good health and is developing normally.

Pathologic Report (Dr. Joseph C. Ehrlich).—Gross Specimen: The specimen measured about 13 by 10 by 11 cm. The outer surface was nodular. On section, it showed a large, partly opened cyst measuring about 10 cm. in its greatest dimension and containing hemorrhagic fluid. Several smaller cysts containing straw-colored fluid were also present. The lining of the large cysts was partly rough and hemorrhagic in color. The lining of the smaller cyst was smooth. Almost half the specimen was occupied by a semisoft, greasy tissue of light yellowish gray. Intermingled with this tissue were fragments of cartilage and bone, with marrow in some instances, suggestive of development of formed bone.

Microscopic Description: Sections revealed a teratoma in which several well differentiated organ tissues were present. These included intestine, stomach, lung, bone and central nervous tissue. In most of these instances the various constituents of the organ were well developed and were integrated in relatively normal fashion. Thus, the intestine appeared with well developed mucosa, lymph follicles, submucosa, muscularis, serosa, blood vessels, nerves and lymphatics in normal relationships. None of the examined sections revealed any evidence of malignant transformation.

SUMMARY

1. A report of a 3 month old infant successfully treated for retroperitoneal teratoma is presented. This is the fifth reported case in infancy and childhood with successful treatment.

2. This case is noteworthy because of the high degree of tissue differentiation present in the pathologic specimen.

975 Walton Avenue (52).

DOUBLE HYDROMETROCOLPOS AND IMPERFORATE ANUS IN A NEWBORN INFANT

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AND
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Abdominal distention in the newborn is infrequent. However, as the result of anomalies of the intestine, cases of complete or partial congenital obstruction do occur. Pneumoperitoneum, rarely observed, caused by rupture of the intestine in utero or at delivery leads to a distended abdomen. A most unusual case in our experience is that of a newborn infant with an enlarged abdomen due to a huge hydrometrocolpos. This is a condition in which a variable amount of fluid, secreted by the uterine cervical glands, collects in the vagina as the result of mechanical obstruction. As suggested by Ladd and Gross,[1] etiologically this is thought to be due to a congenital developmental anomaly. The fluid secreted by the uterine glands varies in quantity and consistency. It is well recognized that during the first few weeks of life there is a normal gray-white discharge from the vagina. The amount of secretion is said to depend on the stimulating estrogen derived from the mother's circulation. When the secretion is small in amount, recognition of the atresia of the vagina may not be possible until later on in life. If there is an abundance of secretion from the uterine cervical glands, resulting in an abdominal mass, attention is drawn to the condition early.

In 1904, Commandeur [2] reviewed the literature on hydrometrocolpos and added a case of his own. Kereszturi,[3] in 1940, described a case in which the condition led to pressure on the urinary tract, resulting in secondary hydroureter and hydronephrosis with ascending infection. Exploratory laparotomy revealed a cystic mass behind the bladder. Pressure on the uterus caused the labial membrane to bulge. Incision of this resulted in the eventual disappearance of the pelvic mass and a return to normal excretion. The same year Mahoney and Chamberlain [4] reported the clinical findings and described the treatment of 4 infants with hydrometrocolpos. As in our patient, 1 child had an imperforate anus requiring a colostomy. In 1942, Richardson and Smart [5] reported a case of a 2 month old infant with an enlarged, distended abdomen for whom the diagnosis of hydro-

From the Children's Surgical Service of Cook County Hospital.

1. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941, p. 385.

2. Commandeur, M.: Imperforation de l'hymen avec hydrocolpos, Bull. Soc. d'obst. de Paris **7**:54, 1904.

3. Kereszturi, C.: Imperforate Hymen Causing Hydrocolpos, Hydro-Ureter, Hydronephrosis and Pyuria: Its Occurrence in Infant, Am. J. Dis. Child. **59**: 1290 (June) 1940.

4. Mahoney, P. J., and Chamberlain, J. W.: Hydrometrocolpos in Infancy, J. Pediat. **17**:772, 1940.

5. Richardson, G. O., and Smart, G. A.: Hydrocolpos in an Infant, Arch. Dis. Childhood **17**:56, 1942.

metrocolpos was not made until autopsy examination. Morris [6] and Rosenblatt and Woolley,[7] in 1943, independently described successful experiences with similar cases. All recommended preliminary aspiration and adequate roentgenologic examination of the hydrometrocolpos with simple incision of the vaginal membrane to release the fluid. In 1 case of Mahoney and Chamberlain autopsy examination revealed a definite obstructing membrane of the vagina above the level of the hymen and, in another instance, Cranwell [8] reported an atresia of the vagina above the normal level of the hymen. In the infant described by Morris an imperforate hymen was observed with a pouch above it. This evidence suggests that hydrometrocolpos is the result of an obstructing membrane of the vagina or an atresia

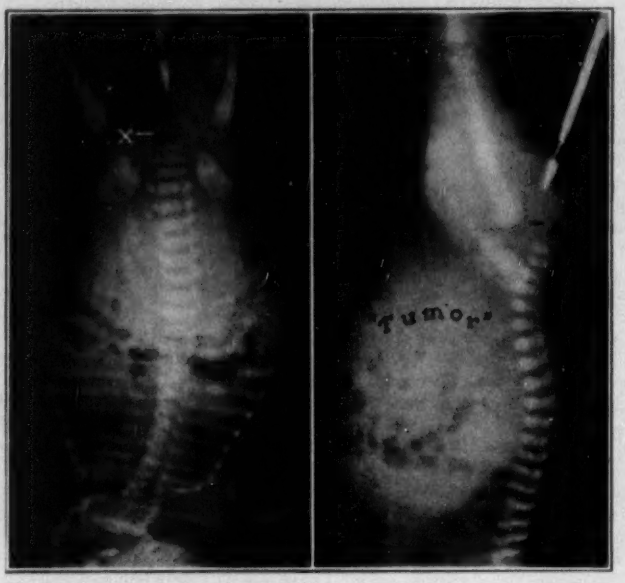

Fig. 1.—Roentgenograms, after the Wangensteen-Rice technic, show the relation of the rectal pouch (*x*) to the marker on the perineum.

of the lower end of the vagina, rather than a secondary condition due to an imperforate hymen.

REPORT OF A CASE

A full term female infant, 10 hours old, was admitted to the surgical ward of the Children's Division of the Cook County Hospital. Severe abdominal distention

6. Morris, P.: Hydrometrocolpos in Infancy: A Cause of Urinary Retention, Intestinal Obstruction, and Edema of the Lower Extremities, Am. J. M. Sc. **210**: 751, 1945.

7. Rosenblatt, M. S., and Woolley, P. V., Jr.: Hydrometrocolpos in Infancy, Ann. Surg. **117**:635, 1943.

8. Cranwell, D. J.: Hydrocolpos congénital, Rev. de gynéc. et de chir. abd., Paris **9**:635, 1905.

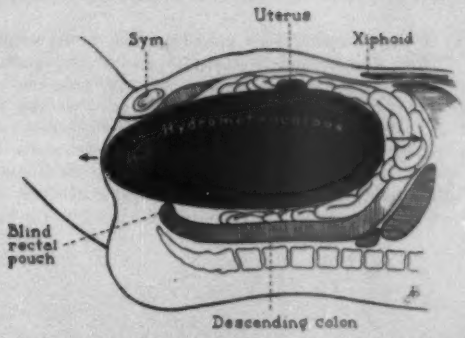

Fig. 2.—Artist's drawing of huge intra-abdominal mass observed at operation.

Fig. 3.—Photograph of surgical specimen which includes (*a*) double uterus, (*b*) left adnexa, (*c*) double vagina and (*d*) glass rod in each cervical os. Septum (*e*) divides "cyst" into two compartments.

was caused by a huge, palpable mass extending from the symphysis pubis to the xiphoid. There was noticeable swelling of the external genitalia, but no vaginal opening was observed in the perineum. An imperforate anus was present. Roentgenologic examination revealed a soft tissue shadow pushing the intestine laterally and up under the diaphragm. After use of the technic described by Wangensteen and Rice, roentgenograms showed the position of the rectal pouch in relation to the anal membrane. Although numerous conditions were considered, the abdominal tumor was not diagnosed preoperatively as hydrometrocolpos. A laparotomy was deemed advisable for exploration of the lesion, as well

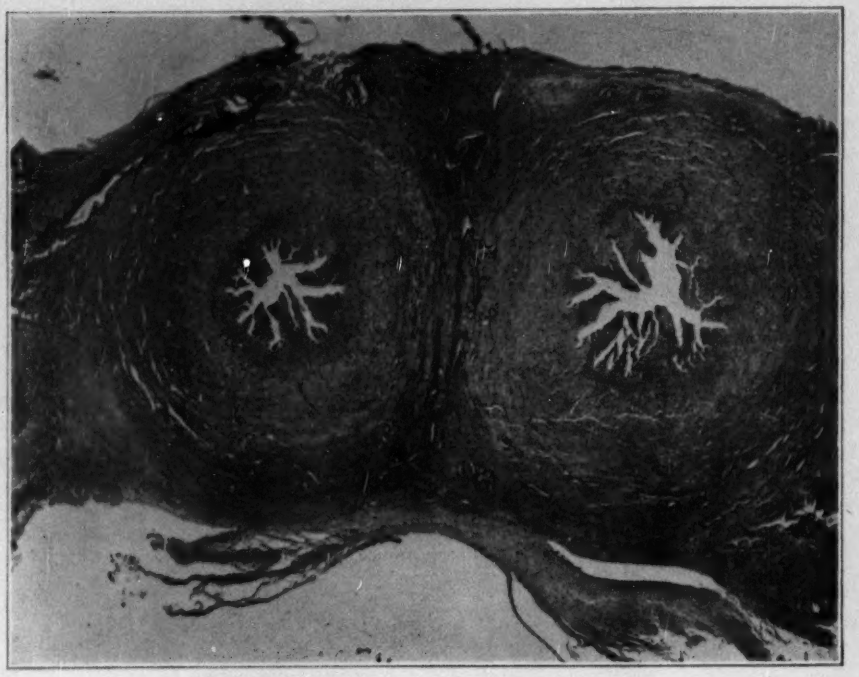

Fig. 4.—Photomicrograph of cross section of double uterus.

as for relief of the obstruction of the colon. At operation a large mass was seen, occupying almost the entire abdomen. The exact nature of the lesion was not apparent, but the possibility of a large sacrococcygeal tumor was considered. The mass was removed intact along with the left adnexa before the pathologic lesion was recognized. A colostomy was performed in the terminal portion of the colon. The patient's postoperative course was uneventful.

Pathologist's Report.—Gross Description: The surgical specimen consisted of an infantile double uterus, left ovary, left fallopian tube and a hugely distended cystic sac, containing 200 to 250 cc. of chalky, watery fluid. An equal amount of fluid had been aspirated during the surgical procedure. The interior of this

cyst was divided equally by a septum, a cervical os opening into each compartment. The lining of the cyst was irregular and purplish gray, while the wall measured 4 to 5 mm. in thickness.

Histologic Description[9]: There were two sections. One was taken transversely through one section of the double infantile uterus. The other was taken through the wall of the large cyst below the uterus.

The section through the wall of the large cyst showed, internally, a slightly convoluted or papillary mucosal structure. The mucosa was covered with a layer

Fig. 5.—Photograph of child with colostomy opening one year after surgical intervention. Note congenital umbilical hernia.

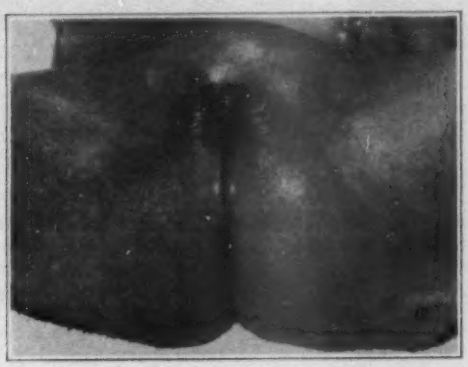

Fig. 6.—Recent photograph of perineum illustrates clitoris and urethra without evidence of vaginal or anal orifice.

of columnar epithelium, and the epithelium was invaginated to form glandular structures which in some respects represented those of the cervix of the adult uterus. The epithelium varied from a nonsecreting columnar cell to a similar, though pale and sometimes vacuolated, cell which apparently had secreting capacities. No ciliated epithelial cells were seen. There was little similarity between the epithelium lining this cyst and the epithelium usually encountered in

9. The histologic examination was made by Dr. George M. Hass, Department of Pathology, the Presbyterian Hospital.

the cervix of the normal infantile uterus. Beneath the epithelium there was an apparent grouping of fibrocytes and mesenchymal cells of undetermined type. These cells seemed immature and in some instances were greatly swollen. Where they were swollen and large, they were restricted to the zones directly beneath the epithelium. The appearance was suggestive of a pseudodecidual reaction. The change in these cells was not quite sufficient to justify a diagnosis of decidual reaction of pregnancy. Beneath the mucosa was a thick fibromuscular wall with abundance of smooth muscle coursing in various directions. This smooth muscle was continuous over a small section of epithelium which was stratified squamous in type and in continuity with the columnar epithelium described previously. It is possible that this represented a sort of junction of an abnormal cervix, a cervical canal and squamous epithelium at the lip of the cervix.

The transverse section through the double uterus showed little dilatation of either uterine horn. The epithelium was thrown up into folds. It was tall columnar in type. The cells were larger and paler than those seen in a normal infantile uterus. The stroma beneath the epithelium, however, was much like that of an infantile uterus. There was nothing suggestive of the pseudodecidual reaction described in the wall of the cyst. The two horns of the uterus were identical in appearance and each showed a fusion of the muscular wall in the midline. The muscular wall elsewhere, however, seemed to be perfect and continued all the way around the lumen of each horn of the uterus.

The diagnosis was congenital hydrometrocolpos and double uterus.

COMMENT

A case is presented of a newborn infant with massive enlargement of the abdomen due to a large hydrometrocolpos, not diagnosed as such preoperatively. A laparotomy was done for relief of the obstruction due to the imperforate anus and for exploration of the abdominal mass.

Cases of hydrometrocolpos appear in the literature, but this case is unusual because of the presence of a double uterus and double vagina without an external opening of the vagina. An imperforate anus was also present. It is believed that the condition is caused by the presence of an imperforate membrane or an atresia of the vagina, due to arrested embryologic development. There is an abundant secretion of the uterine cervical glands, stimulated by the estrogenic substance absorbed from the maternal circulation. The amount secreted determines the size of the hydrometrocolpos. If the nature of the condition is recognized, surgical treatment consists of incision and drainage of the vagina in order to remove the fluid. The "tumor" disappears following the drainage of the dilated vagina. In this case both compartments of the vagina would have been drained. Unnecessary surgical intervention will be avoided if the pathologic changes are recognized early.

1753 West Congress (12).

MESOTHELIOMA OF THE PLEURA IN A CHILD

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B. CARL RUSSUM, M.D.

AND

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OMAHA

The occurrence of a primary mesothelioma of the pleura in a child 19 months of age has prompted us to review the literature briefly and to present a clinical and postmortem report on this single patient.

In 1870, Wagner [1] first described a tubercle-like lymphadenoma of the pleura which Schulz [2] later reexamined and described as endothelial carcinoma. Since that time, at least 250 case reports have appeared in the literature. Klemperer and Rabin [3] in a review of mesothelial tumors found more than thirty different names for this type of tumor. Most European authors referred to the neoplasm as "celothelioma," while Ewing [4] classified it as endothelioma, Yater [5] as endothelial carcinoma and Geschickter [6] as mesothelioma.

As has been pointed out elsewhere,[7] the splanchnocele of the embryo gives rise to the serous cavities (pleural, pericardial and peritoneal), which are lined with persisting celomic epithelium or mesothelium. Splanchnocelic derivatives show persisting celomic epithelium, and the underlying mesoderm forms vascular connective tissue. Tumors originating in the pleura and called "mesothelioma" exhibit similar tendencies, with epithelial and fibrous constituents. In this paper, therefore, the name "mesothelioma" will be used.

From the Departments of Pathology and Pediatrics, The Creighton University School of Medicine and St. Catherine's Hospital.

Abstracted from a thesis presented by Dr. Reals to The Creighton University for the degree of Master of Science in Pathology.

1. Wagner, E.: Das tuberkelähnliche Lymphadenom, Arch. d. Heilk. **11**:497, 1870.

2. Schulz, R.: Das Endothelcarcinom, Arch. d. Heilk. **17**:1, 1875.

3. Klemperer, P., and Rabin, C. B.: Primary Neoplasms of the Pleura; Report of Five Cases, Arch. Path. **11**:385 (March) 1931.

4. Ewing, J.: Neoplastic Diseases; A Treatise on Tumors, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

5. Yater, W. M.: Tumors of the Heart and Pericardium; Pathology, Symptomatology and Report of Nine Cases, Arch. Int. Med. **48**:627 (Oct.) 1931.

6. Geschickter, C. F.: Mesothelial Tumors, Am. J. Cancer **26**:378, 1936.

7. Reals, W. J.; Russum, B. C., and Walsh, E. M.: Primary Mesothelioma of the Pericardium, Arch. Path. **44**:380 (Oct.) 1947.

Cancer in children under 14 years of age is not uncommon. However, Dargeon [8] did not mention mesotheliomas in his reviews, although tumors of the soft somatic tissues were indicated as the fifth most frequent site of malignancy in a list of six, and primary pleural tumors would presumably be classified under that heading. In the numerous reviews of primary pleural mesotheliomas, the average age of incidence falls in the fifth and sixth decades of life. The youngest patient, a boy of 5 years, was reported on as early as 1904 by von Hibler [9] from Germany and his report was cited by Ewing.[4]

REPORT OF A CASE

W. S., a white boy 14 months of age, was first admitted to St. Catherine's Hospital, on the service of one of us (W. J. E.), April 10, 1944, for acute dyspnea following accidental inspiration of two pennies. A roentgenogram of the chest revealed the pennies in the upper part of the trachea, with no pulmonary changes or pleural thickening. The pennies were removed, and the child was dismissed from the hospital on the next day.

He was readmitted five months later because of cough for six days and irritability with fever for two days. The cough had begun suddenly and was paroxysmal. The mother stated that the coughing episodes were apparently precipitated when the child was held in her arms in such a way that the right side of his chest was pressed to the mother's body. While sleeping, the child consistently lay on his left side. He had also been irritable, and the skin had seemed "feverish." The day before his admittance to the hospital, there had been spells of severe coughing and the child had refused to eat.

The child was the first born of healthy parents. The birth was at full term and without complications. He was breast fed until 5 months of age and then given a formula which was well taken. Growth and development had apparently been normal. There was no family history of malignant disease. Both parents were in good health. There were no siblings.

Physical examination on his admission revealed a well developed, well nourished, dyspneic child 19 months of age. The skin was pale and abnormally warm. The temperature was 102 F. There were no abnormalities of the head and neck. The heart sounds were rapid and distant.

The entire left side of the chest did not move on respiration, while the percussion note was dull and breath sounds were absent in front and back. The right side of the chest seemed normal. The respiratory rate was 60. The abdomen, extremities and reflexes were normal.

On his admission the urine was normal; the hemoglobin concentration was 65 per cent, the red blood cell count 3,350,000 and the white blood cell count 9,800, with 35 per cent lymphocytes and 65 per cent neutrophils.

The roentgenograms of the chest on his admission revealed a completely opaque left pulmonary field. The heart was pushed to the right but the right pulmonary field was clear (fig. 1).

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8. Dargeon, H. W., in Discussion on Tumors, Benign and Malignant, J. Pediat. **30**:716, 1947; Cancer in Childhood, St. Louis, C. V. Mosby Company, 1940; Cancer in Childhood from Birth to Fourteen Years of Age, J. A. M. A. **136**:459 (Feb. 14) 1948.

9. von Hibler: Endothelkrebs der Pleura im Kindesalter, Jahrb. f. Kinderh. **59**:367, 1904.

The day after his admission 100 cc. of bloody nonpurulent fluid was withdrawn from the left side of the chest. No tumor cells or acid-fast organisms were observed in the centrifuged sediment of this material, and cultures were sterile. After the paracentesis, the mediastinum was still shifted to the right and increased density could now be seen at the base of the left lung. The child was then given sulfamerazine therapy, but the drug proved ineffective and its use was discontinued.

On the thirteenth day in the hospital the pronounced shift of the mediastinum to the right was evident. The liver was palpable 5 cm. below the right costal margin and the spleen was palpable. Cyanosis and respiratory embarrassment gradually became severer, although a total of 3,100 cc. of bloody fluid was removed from the chest on repeated taps. The hemoglobin concentration fell to 32 per cent and the red blood cell count to 2,500,000, although two transfusions of whole blood were given. The child was placed in an oxygen tent terminally but died, apparently of suffocation, on the fortieth day in the hospital.

Fig. 1.—Opaque left pulmonary field, with mediastinal shift and displacement of heart to right.

Observations at Autopsy.—The autopsy was performed three hours after death by Dr. F. J. Campos. The body was that of a well developed, emaciated white male child, with distention of the abdomen.

The principal observations were of the thorax and abdomen. The left lung was compressed against the mediastinum by a firm white tumor mass, measuring 7 cm., which had apparently arisen from the left parietal pleura just above the leaf of the diaphragm. The entire left visceral and parietal pleura was thickened and involved by this tumor. The large tumor mass was white and firm, but on section its center was soft and contained about 10 cc. of murky fluid. The remainder of the growth was firm, white and homogeneous. The underlying lung was partially atelectatic but was not infiltrated by the neoplasm. The hilar nodes were normal. The heart and great vessels were shifted to the right but were otherwise unchanged. The right lung was crepitant; there were a few petechiae over the pleura but no involvement with the tumor. The right and left lungs, tumor, heart and great vessels together weighed 675 Gm.

The liver was displaced downward and mottled red-yellow but was not invaded by the tumor. There was only passive hyperemia of the remaining abdominal viscera.

Permission to examine the cranium was denied by the parents.

Fig. 2.—Upper, large tumor encasing left lung. Lower, large tumor of left pleura after removal of lung.

The anatomic diagnosis was primary mesothelioma of the left visceral and parietal pleura, with compression atelectasis of the left lung; mediastinal shift to the right; petechial hemorrhages into the right pleura; fatty metamorphosis of the liver; passive congestion of spleen, kidneys, and entire gastrointestinal tract, and severe emaciation.

Microscopic Observations.—Microscopic studies were made on sections stained with hematoxylin and eosin, by the azocarmine method for connective tissue, by Foot's method for reticulum, with Masson's trichrome method and by orcein and hematoxylin stains. Sections of the tumor mass and of the thickened pleura revealed irregular, round tumor cells growing in a fibrous stroma, with complete destruction of the pleural architecture. The tumor was highly cellular, and there was considerable pleomorphism. The cells grew in columns and cords surrounded by a fine fibrous stroma. Only a few blood vessels could be identified in the tumor, although a number of dilated capillaries could be seen at the extreme margin. Mitotic figures were numerous. The nuclei were large and prominent nucleoli could be seen in many cells. There was no suggestion of acinar formation. The supporting stroma consisted of a fine argentaffin intercellular network. Multiple sections through the testes, thymus, thyroid, adrenal glands, pancreas, kidneys, both lungs and the gastrointestinal tract revealed no other evidence of tumor formation.

Fig. 3.—Photomicrograph of tumor; × 160.

COMMENT

A comprehensive review of the literature revealed no report of mesothelioma in a patient as young as the one we have described—19 months of age. The earliest instance heretofore was recorded by von Hibler [9] in a 5½ year old white boy. His patient also complained of dyspnea, and he lived only five weeks after the onset of symptoms; during his stay in the hospital 2,500 cc. of blood-tinged fluid was removed from the chest, but no tumor cells could be identified in the sediment. The tumor described at autopsy was grossly similar to that in our patient, and the microscopic observation of "fibrous tissue with masses of epithelial cells infiltrating" parallels our observations.

The clinical picture is variable, but of some diagnostic importance is the rapid reaccumulation of bloody fluid after thoracentesis. The demonstration of tumor cells either on paraffin sections of the embedded sediment or by the Papanicolaou technic would be extremely helpful. However, tumor cells and desquamated mesothelia tend to undergo rapid degeneration in the fluid, rendering microscopic

interpretation difficult.[10] Bulging of the intercostal spaces, contralateral shift of the mediastinum and absence of breath sounds over the affected side are the usual physical findings. Roentgenograms may show the mediastinal shift, the fluid level and, in some instances, the thickened pleura.

SUMMARY

Mesothelioma of the pleura in children is uncommon. The present patient, a 19 month old child, is the youngest so far recorded.

The diagnosis is difficult, but bulging of the intercostal spaces, contralateral shift of the mediastinum and rapid reaccumulation of bloody fluid after paracentesis are helpful differential points.

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Progress in Pediatrics

CONGENITAL ABSENCE OF THE ABDOMINAL MUSCLES

Associated with Malformation of the Genitourinary and Alimentary Tracts; Report of Cases and Review of Literature

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CINCINNATI

CONGENITAL absence of the abdominal muscles is a rare malformation; the absence of an entire muscle group is less common than that of individual muscles, and bilateral involvement is less common than unilateral. Absence of muscles of the lower part of the trunk or of the extremities has been reported infrequently in the literature. The most commonly described defects are in the pectoral muscles. In Bing's [1] collection 102 cases of absence of the pectoral muscles were recorded, in contrast to the relatively small number of instances in which other muscles, including the abdominal, were absent. According to Baxter,[2] 186 cases of congenital defects of the pectoral muscles had been reported by 1909, in comparison with 11 cases of deficiency of the abdominal muscles.

A total of 45 cases of congenital absence of the abdominal muscles has been reported to date. Congenital anomalies of the genitourinary tract have been recognized in association with these muscular defects since the earliest reports.[3] It is our purpose to add 3 new cases to

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1. Bing, R.: Ueber angeborne Muskeldefecte, Arch. f. path. Anat. **170**:175, 1902.

2. Baxter, E. H.: Congenital Absence of the Abdominal Muscles: Case Reports, Ohio State M. J. **28**:840, 1932.

3. (*a*) Henderson, B.: Congenital Absence of Abdominal Muscles, Glasgow M. J. **33**:63, 1890. (*b*) Parker, R. W.: Absence of Abdominal Muscles in an Infant, Lancet **1**:1252, 1895. (*c*) Guthrie, L.: Case of Congenital Deficiency of the Abdominal Muscles with Dilatation and Hypertrophy of the Bladder and Ureters, Tr. Path. Soc. London **47**:139, 1896. (*d*) Platt, W. B.: A Rare Case of Deficiency of the Abdominal Muscles, Philadelphia M. J. **1**:738, 1898. (*e*) Osler, W.: Congenital Absence of the Abdominal Muscles, with Distended and Hypertrophied Urinary Bladder, Bull. Johns Hopkins Hosp. **12**:331, 1901. (*f*) Stumme, E. G.: Ueber die symmetrischen kongenitalen Bauchmuskeldefekte und über die Kombination derselben mit anderen Bildungsanomalien des Rumpfes (Hochstand, Hypertrophie und Dilatation der Blase, Ureterendilatation, Kryptorchismus, Furchennabel, Thoraxdeformität, uzw.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. **11**:548, 1903.

TABLE 1.—*Reported Cases of Congeni*

	Authors	Year	Sex	Age	Abdominal Muscles—Results of Postmortem Examination or Electrical Stimulation					
					Rectus	Obliquus Externus	Obliquus Internus	Transversus	Umbilicus	Thorax
1	Fröhlich [4]	1830	M	Child	Present	Defect of "lateral abdominal muscles"			.....	Pigeon breast
2	von Ammon [5]	1842	M	Child	Lower half absent	Muscles developed at puberty			.....	.....
3	Henderson [24]	1890	M	60 yr.	Lower half absent	Deficient			.....	.....
4	Parker [25]	1895	M	Newborn	Trace	Rudimentary	Rudimentary	Absent	Scar	.....
5	Guthrie [26]	1896	M	9 wk.	Absent	Trace	Trace	Trace	Groove	Pigeon breast
6	Platt [26]	1896	M	2 yr.	Present	Present	Uncertain	Absent	Slit	.....
7	Osler [26]	1901	M	6 yr.	Lower half absent	Absent	Absent	Absent	Furrow	Harrison's groove
8	Stumme [27]	1903	M	17 yr.	Lower half absent	Feeble	Absent	Present	Scar	Harrison's groove
9	Garrod and Davies [28]	1906	M	5 mo.	Rudimentary				Scar	Sternum upward and forward
10	Bolton, C.: Tr. Clin. Soc. London **39**:347, 1906	1906	M	9 mo.	Present	Absent	Absent	Absent	.....	.....
11	Hall [19]	1907	M	3 wk.	Lower half absent; upper half thin	Partial	Partial	A few fibers	Imperfect	.....
12	Hall [19]	1907	M	2 wk.	Lower half absent; upper half thin	Thin	Thin	A few fibers	Depression	.....
13	Peis-Leusden [21]	1908	M	3 mo.	Trace	Absent	Absent	Absent	Normal	Anterior portion bulging
14	Peis-Leusden [21]	1908	M	7 wk.	Present	?	?	?	Normal	Flattened laterally
15	Levy, R.: Beitr. z. klin. Chir. **57**:201, 1908	1908	M	70 yr.	Lower half absent	Partial	Right present; left absent	?	.....	.....
16	Mollison [22]	1909	M	2 yr.	No response to electrical stimulation				.....	.....
16a	Mackeith and others [23]	1923	M	16 yr.	Same patient as 16				.....	.....
17	Smith, E. B.: Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) **6**:150, 1913	1913	?	2 mo.	Absent	Absent	Absent	Absent	Longitudinal groove	.....
18	Thatcher [23]	1913	M	3 wk.	Trace	Absent	Absent	Absent	Longitudinal furrow	Short and wide
19	Stern, A.: Arch. Diagn. **8**:73, 1915	1915	?	6 wk.	Absent	Absent	Absent	Absent	.....	.....
20	Eckhoff [29]	1923	M	10 days	Lower half absent	Sheet of muscle fibers	A few strips	Present	.....	Narrowed; Harrison's groove

tal Absence of the Abdominal Muscles

Testes	Kidneys	Ureters	Bladder	Urethra	Gastrointestinal Anomaly or Other Abnormality	Living or Dead	Cause of Death	Post-mortem Examination
Descended	.....	.....	.....	.....	.....	L	.....	.....
.....	.....	.....	.....	.....	.....	L	.....	.....
Undescended	.....	.....	.....	.....	A mammary gland on right abdominal wall	L	.....	.....
Undescended	Enlarged; hydronephrosis	Dilated; hypertrophied	Hypertrophied	No obstruction	Latissimus dorsi slightly developed	D	Collapse and emphysema	Done
.....	Infected	Dilated	Hypertrophied; fixed to umbilicus	.....	Quadratus lumborum rudimentary	D	Wasting	Done
Undescended	Not palpable	.....	Not palpable	.....	.....	L	.....	.....
Undescended	Palpable	.....	Extended to navel	.....	.....	L	.....	.....
Undescended	Right enlarged; left small	Dilated	Large; adherent to umbilicus	No obstruction	Mesocecum noticeably long	L	.....	.....
Undescended	Right very small; left >normal	Right normal; left dilated	Hypertrophied; attached to umbilicus	.....	Quadratus lumborum thin	D	Erysipelas and bronchopneumonia	Done
Undescended	.....	.....	.....	.....	.....	D	Intercurrent infection	Not done
Undescended	Right >left	Dilated	Hypertrophied; dilated	No obstruction	.....	D	Furunculosis; suppurative pericarditis	Done
Undescended	Hydronephrosis	Greatly dilated	Pronounced contraction	No obstruction	Quadratus lumborum thin	D	Unknown, sudden death	Done
Undescended	Left normal; right small	Left tortuous; right dilated distally	Hypertrophied	No obstruction	.....	D	Peritonitis	Done
Undescended	.....	.....	.....	.....	Inguinal hernia	L	.....	.....
Undescended	.....	.....	.....	.....	Inguinal hernia	L	.....	.....
Undescended	.....	.....	No distention	.....	.....	L	.....	.....
.....	.....	.....	Repeated infection	.....	.....	L	.....	.....
.....	.....	.....	Palpable above pubis	.....	Flexion deformity of right leg and thigh; genu valgum; talipes calcaneo-valgus, bilateral	L	.....	.....
Undescended	Right hydronephrosis; left normal	Dilated	Dilated; hypertrophied	.....	Congenital dislocation of hips	D	Bronchopneumonia	Done
.....	.....	.....	Enlarged	.....	.....	L	.....	.....
Undescended	Hydronephrosis	Dilated	Hypertrophied	No obstruction	Stomach on right; cecum and appendix immediately below; ascending colon lay transversely above bladder; transverse colon behind ascending colon	D	Diarrhea	Done

TABLE 1.—*Reported Cases of Congenital Ab*

	Authors	Year	Sex	Age	Abdominal Muscles—Results of Postmortem Examination or Electrical Stimulation				Umbilicus	Thorax
					Rectus	Obliquus Externus	Obliquus Internus	Transversus		
21	Blasi [11]	1927	M	2½ mo.	? Present	Absent	Absent	Absent	.....	Narrowed
22	Ikeda and Stoesser [12]	1927	M	5 mo.	Absent	Absent	Absent	Absent	Linear scar	Sternum forward
23	Tailliens [26]	1928	M	2½ mo.	Upper half poor; lower half fair	Partial	Partial	Absent	.....	.....
24	Brindeau and Jacquet [13]	1928	M	2 mo.	Present	Absent	Absent	Absent	Slit with ulcer	Narrow and prominent
25	Fletcher [9]	1929	F	Newborn	Incomplete	?	?	?	.....	.....
26	Poli, A: Arch. di ortop. 45: 775, 1929	1929	M	3 mo.	No response to electrical stimulation				Normal	Normal
27	Hofstein [7]	1930	F	Newborn	No response to electrical stimulation				Normal	Elevated
28	Monerieff [15]	1931	M	6 mo.	A few strands	Absent	Absent	Absent	Slit	Deformed
29	Malossi, C., and Gelli, G.: Lattante 2: 101, 1931	1931	M	10 mo.	Lower half absent; upper trace	Absent	Absent	Absent	Slit	Sternum projected; costal angle obtuse
30	Baxter [2]	1932	M	4 wk.	.....	.....	.....	.....	Slit	Short and elevated
31	Baxter [2]	1932	M	17 yr.	.....	.....	.....	.....	Difficult to locate	Harrison's grooves
32	Baxter [2]	1932	M	6 wk.	Defect on left side				.....	.....
33	Friedley, R. S., in discussion on Baxter [2]	1932	M	1 yr.	Few muscle fibers present				.....	.....
34	Stoesser, A. V.: Arch. Pediat. 50: 739, 1933	1933	M	Newborn	.....	.....	.....	.....	.....	Normal
35	Parsons, L. G., and Barling, S.: Diseases of Infancy and Childhood, London, Oxford University Press, 1933, vol. 2, p. 1404	1933	?	6 mo.	.....	.....	.....	.....	.....	.....
36	McClendon, S. J.: Arch. Pediat. 51: 673, 1934	1934	M	6 mo.	Absent	Absent	Absent	A few fibers	.....	.....
37	Housden [8]	1934	M	Newborn	Absent	Partial	Absent	Absent	Normal	Pigeon breast
38	Gibbens, J.: Brit. J. Child. Dis. 31: 45, 1934	1934	M	2 mo.	Absent	Absent	Absent	Absent	.....	.....
39	Lichtenstein [14]	1939	M	2 yr.	Absent	Absent	Absent	Absent	.....	Pigeon breast
40	Howard [9]	1940	M	Newborn (1 of twins)	Thin	Thin	Thin	Thin	.....	.....
41	Howard [9]	1940	M	Newborn	Absent	Absent	Absent	Absent	.....	.....
42	Aldrich [27a]	1942	M	5 wk.	Absent	Absent	Absent	Present	.....	.....
43	Daut and others [16]	1947	M	3½ yr.	Abdominal wall thin; muscles not tested				.....	.....
44	Irvin and Kraus [16]	1948	M	2 wk.	Briefly described to be without muscles				.....	.....
45	Obrinsky [27b]	1949	M	5½ mo.	Present	Poorly developed			.....	Narrow; short

sence of the Abdominal Muscles—Continued

Testes	Kidneys	Ureters	Bladder	Urethra	Gastrointestinal Anomaly or Other Abnormality	Living or Dead	Causes of Death	Post-mortem Examination
.....	Right palpable (urine normal)	.....	.....	.....	Megacolon	L	.....	.....
Undescended	Left kidney small	Not dilated	Hypertrophied; adherent to umbilicus	No obstruction	Appendix free	D	Pneumonia	Done
.....	.....	.....	.....	.....	.....	D	Diarrhea and malnutrition	Done
Undescended	.....	.....	.....	.....	Valgus deformity of feet	L	.....	.....
.....	.....	.....	.....	.....	.....	D	Inanition	Not done
Undescended	Palpable	.....	Hypertrophied; dilated	.....	.....	L	.....	.....
.....	.....	.....	.....	.....	.....	L	.....	.....
Undescended	Enlarged	Dilated	Adherent to abdominal wall	No obstruction	Meckel's diverticulum; cecum on left side	D	Pneumonia	Done
.....	Hydronephrosis; atrophy of kidneys	Dilated	Hypertrophied	No obstruction	.....	D	Respiratory infection	Done
Undescended	.....	.....	Hypertrophied	.....	Double talipes equinovarus	D	Pneumonia	Done
Undescended	.....	.....	Hypertrophied	.....	Extreme retraction of neck and head	L	.....	.....
	Genitourinary tract normal				.....	L	.....	.....
.....	Enlarged	Dilated; mucosal folds	Enlarged	.....	.....	D	Uremia	Done
Undescended	.....	.....	Hypertrophied	.....	.....	D	Exfoliative dermatitis	Not done
.....	.....	.....	.....	.....	.....	D	Pulmonary infection	Not done
.....	Hydronephrosis; atrophy of kidney	Left dilated	Dilated	.....	.....	D	Septicemia	Done
Undescended	Hydronephrosis	Dilated	Hard tumor	Prostatic hypertrophy	Spina bifida occulta; quadratus lumborum absent; talipes equinovarus	D	Uremia	Done
Undescended	.....	Dilated	Dilated; hypertrophied	No obstruction	.....	D	Diarrhea	Done
Undescended	Hydronephrosis	Dilated	Dilated; hypertrophied	No obstruction	Cecum and appendix near midline; cecum, appendix, ascending colon and ileum had common mesentery	D	Bronchopneumonia; peritonitis	Done
Undescended	Normal	Atresia	Dilated; hypertrophied	Atresia	.....	D	?	Done
Undescended	Cystic degeneration	Atresia below; dilated above	Hypertrophied	.....	Bilateral talipes equinovarus	D	?	Done
Undescended	Hydronephrotic; cystic	Dilated; tortuous	Hypertrophied	Diverticulum in prostatic urethra	.....	D	Malnutrition	Done
Undescended	Nonfunctioning left kidney	Dilated	Greatly dilated	.....	.....	L	.....	.....
.....	Hydronephrosis	Patent but narrow	Dilated; hypertrophied	No obstruction	Gallbladder in abnormal position; entire colon had a free mesentery	D	Bronchopneumonia	Done
Undescended	Left polycystic	Right dilated	Dilated; hypertrophied	Diverticulum	Right 4th toe nail absent	D	Urinary infection	Done

the series and to describe an additional associated anomaly of the alimentary tract.

I. REVIEW OF LITERATURE

The order of frequency with which the various abdominal muscles are absent is as follows: (1) transversus abdominis, (2) the rectus abdominis below the umbilicus, (3) obliquus internus abdominis, (4) obliquus externus abdominis and (5) the rectus abdominis above the umbilicus.

The thin sheetlike muscles, the obliquus and the transversus, are absent more frequently than the stronger and thicker rectus muscles. When the latter group is affected, the deficiency is usually in the portion below the umbilicus.

Although the terms "absence" and "agenesis" of the abdominal muscles are commonly used, most of the cases seem to be characterized by extreme deficiency of the abdominal muscles, instead of by complete absence of the musculature. Whether these cases represent atrophy of normally developed muscles or a primary developmental defect has not been clearly determined.

The earliest reports of congenital absence of the abdominal muscles were those of Fröhlich [4] in 1839, von Ammon [5] in 1842 and Henderson [3a] in 1890. Reports of special interest are briefly abstracted later; data from the remainder are recorded in table 1. Fröhlich [4] described a male child presenting a defect of the lateral abdominal muscles and pigeon breast deformity of the thorax. The recti were present. The condition of the urinary tract was not mentioned. The testes were said to be in the scrotum. Von Ammon's [5] patient was a male child with deficiency of the lower segment of the recti and other muscles of the lower part of the abdominal wall. The bladder was not described. The defective muscles were said to have developed into normal muscles about the time of puberty. According to Henderson's [3a] report, his patient was a man, aged 60, presenting a large prominence in the lower part of the abdomen due to congenital weakness of the abdominal wall. The recti were fairly well developed in the upper part but ended in a narrow tendon in the lower part. Protrusions on each side of the abdomen made it possible to see the movements of the intestinal loops. The scrotum was not developed, and the testes were undescended.

These three early reports were brief and apparently described mild types of this congenital anomaly of the abdominal muscles. Fröhlich's patient is the only one in the literature with descended testes.

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4. Fröhlich, F.: (*a*) Der Mangel der Muskeln, insbesondere der Seitenbauchmuskeln, Würzburg, C. A. Zurn, 1839; (*b*) cited by Housden, L. G.: Arch. Dis. Childhood **9**:219, 1934.

5. von Ammon, F. A.: Die angebornen chirurgischen Krankheiten des Menschen in Abbildungen dargestellt und durch erläuternden Text erklärt, Berlin, F. A. Herbig, 1842, p. 59; cited by Housden.[4b]

SEX INCIDENCE

It is of particular interest that congenital absence of the abdominal muscles is rarely observed in the female. Only 2 cases have been reported to date. The first, reported by Fletcher [6] in 1928, concerned a prematurely born girl, weighing 2,700 Gm. Her abdomen was pedunculated like a large tumor and was covered only by thin parchment-like parietal peritoneum through which the abdominal viscera could be seen. In the hypogastric region, a trace of rectus muscle was present. Death due to inanition occurred after twenty-four days. Necropsy was not performed. The parents were first cousins. Unfortunately, this report was brief and incomplete, without record of associated anomalies. The defect was obviously a massive omphalocele, but the muscle deficiency was greater than that generally described.

The second case was described by Hofstein [7] in 1930. This newborn female infant was the firstborn of 6 children; none of the siblings had any congenital anomalies. The parents were healthy. Immediately after her birth, attention was directed to the infant's abdomen, which was flaccid and spread out laterally and was thrown into transverse striations with the child in the sitting position. The thin abdominal wall permitted one to see the pattern of the abdominal organs. After the child nursed, the stomach was perfectly outlined beneath the abdominal wall. The umbilicus was normal. The thoracic cage was elevated, and respiration was of the thoracic type. Inspiratory retraction of the substernal region was prominent. Roentgenographic examination of the chest revealed a flat diaphragm. Electrical stimulation of the abdominal wall provoked no contraction of abdominal muscles. The general condition of the patient was good. This female infant apparently did not have the usual finding of an associated anomaly of the genitourinary tract. The subsequent course is unknown.

ANOMALIES OF THE GENITOURINARY TRACT

Parker [5b] in 1895 reported the first case associated with anomalies of the urinary tract. The patient was a full term male infant. The weight at birth was 5½ pounds (2,495 Gm.). A large and flaccid abdomen was the most significant sign, and it was possible to feel the visceral organs through the thin wall. The umbilicus appeared normal in position but resembled a linear scar. Death was due to collapse and emphysema of the lungs. At necropsy a few muscle fibers were noted to represent the obliquus externus and internus abdominis muscles

6. Fletcher, W. M. A.: Congenital Absence of the Abdominal Wall, M. J. Australia **1**:435, 1928.

7. Hofstein, J.: Absence congénitale des muscles abdominaux chez un nouveau-né du sexe féminin, Gynéc. et obst. **22**:23, 1930.

on each side. The testes were undescended. The bladder, which was situated entirely in the abdominal cavity, was hypertrophied. The urethra was not obstructed. Both ureters and the renal pelves were patent. The kidneys were enlarged. The stomach and intestine were normal.

Stumme [8] in 1903 reported the case of a boy who was able to live to puberty despite an associated anomaly of the genitourinary tract and repeated bouts of urinary tract infection. The patient was born of normal healthy parents and had a normal birth history. The testes were noted to be undescended at birth and the navel drained for two weeks during the neonatal period. Except for a severe attack of "inflammation of the lungs" in early infancy and measles, scarlet fever and diphtheria in early childhood, his past history was without significance. At the age of 15 years, the patient began to experience pressure pains on both sides of the abdomen in the region of the hypochondrium, for which he received various treatments with no response. He was first seen by Stumme at 17 years of age in 1901, when he was observed to be a medium-sized poorly nourished boy. The thorax was very flat; the sternum was depressed at the level of the sixth rib, and the xiphoid process projected forward. Harrison's groove was present on both sides. The abdomen showed the usual wavelike appearance with a thin wall and visible intestinal patterns. Longitudinal and vertical lines or furrows were present in the skin of the abdominal wall. The navel was in the form of a central depression. Electrical stimulation tests revealed the presence of the rectus muscles above the navel; the rectus muscles below the navel were extremely weak. The external oblique muscle was present but weak; the internal oblique muscle was lacking entirely. The quadratus lumborum was strong. A roentgenogram of the thorax showed a slightly flattened diaphragmatic arch. The scrotum consisted of two small tabs of skin without evidence of a raphe. The testes were undescended.

Fever, abdominal pain on the left radiating to the back and pyuria led to the diagnosis of left-sided pyelonephritis. Cystoscopic examination revealed a deep fold in the anterior wall of the bladder and displacement of the ureteral orifices so that they lay opposite each other almost in a straight line. An exploratory laparotomy was performed in January 1902. The bladder was observed to be partially connected with the anterior abdominal wall by a firm, cordlike urachal remnant which was severed. The left ureter was dilated and tortuous; the left kidney was small but in normal position. The right ureter was slightly tortuous, and the right kidney was twice its normal size. During the operation palpation of the gastrointestinal tract revealed a noticeably long mesocecum. After operation, the fold in the anterior wall of the bladder disappeared and the ureteral orifices assumed their

normal relationships. Postoperatively, the patient had a protracted stormy course with periods of fever, chills and urinary symptoms but finally recovered. Stumme concluded that the attachment of the urachus might account for the obstruction of the intramural portion of the ureters and of the vesical end of the urethra.

Housden [8] also called attention to the presence of congenital urethral obstruction as a possible cause of the genitourinary anomaly encountered in these cases. His patient was a male newborn infant. The mother had polyhydramnios in the latter part of pregnancy. The birth history was normal, and the weight at birth was 7½ pounds (3,402 Gm.). The child's abdominal wall was thin, wrinkled and thrown into folds. The umbilicus appeared to be normal. The bladder was felt as a hard tumor extending upward beyond the umbilicus. Both kidneys were palpable. Other associated conditions were talipes equinovarus of the right foot, pigeon breast deformity of the thorax, spina bifida occulta and undescended testes. The infant died of uremia on the twenty-sixth day of life.

Necropsy revealed a short bundle of muscle fibers representing part of the left external oblique muscle, while the rest of the abdominal muscles were absent. The quadratus lumborum was also lacking. Hypertrophy of the bladder, bilateral hydronephrosis and pyelectasis were the most prominent observations. The upper part of the prostatic urethra was greatly dilated, while the lower portion was hypertrophied. A prominent longitudinal ridge was seen to be projecting into the lumen of the urethra. The projection was thought to be responsible for the obstructive uropathy. However, during life there was no gross evidence of obstruction of the urinary flow. A catheter was passed into the bladder with ease, and injected contrast medium passed out readily without any sign of obstruction.

Howard [9] in 1940 described another interesting observation in his case. The patient was a male newborn infant, the second of twins, with a weight at birth of 1,760 Gm., who lived for five hours. Necropsy showed all muscle layers to be thin but present. Both testes were undescended. The right kidney weighed 5 Gm. (normal weight 15 Gm.) but was normal in position. The capsule was studded with many cystic structures. The pelvis was poorly defined; the right ureteropelvic junction could not be identified. The right ureter was tortuous and thickened, and the lower two thirds showed complete obliteration of the lumen. The left kidney weighed 5 Gm.; cystic formation was present. The left ureter was described as a "thin fibrotic structure with

8. Housden, L. G.: Congenital Absence of the Abdominal Muscles, Arch. Dis. Childhood **9**:219, 1934.

9. Howard, P. J.: Congenital Absence of the Abdominal Muscles and Genitourinary Malformation: Report of 2 Cases, Am. J. Dis. Child. **60**:669 (Sept.) 1940.

maximum diameter of 4 mm." and had no lumen. The bladder was greatly hypertrophied. A probe could be introduced into the ureter on each side to a depth of approximately 4 mm. The proximal part of the urethra was patent for a length of 2 cm. On section congenital atresia of the urethra was seen beyond this point.

The following abstract of the case report of Daut and his associates [10] is of interest with respect to the last three reports, since obstruction was diagnosed during life and apparently responded to surgical intervention.

A male child 3½ years of age was admitted to the Mayo Clinic on May 16, 1945 because of (1) constant dribbling of urine, (2) recurring episodes of fever and (3) lack of abdominal muscles. He manifested the usual triad of a large and flaccid abdomen, undescended testes and symptoms of urinary infection. A complete urologic examination disclosed moderate pyelectasis of the right side, fairly good function of the right kidney, a nonfunctioning left kidney and a greatly dilated bladder. Cystoscopic examination revealed a moderately hypertrophied interureteric bar and some redundant tissue in the region of the vesical neck.

Since it was believed that the urinary retention might be based on an imbalance of the detrusor urinae muscle and the vesical neck, a perineal transurethral resection of the vesical neck was performed. Thirty small pieces of tissue weighing a total of 3 Gm. were removed from the entire circumference of the vesical neck and the hypertrophied interureteric bar.

Eight months after operation the patient's condition was noted to be greatly improved. His bladder function was almost normal. Dribbling of urine occurred occasionally. The severity of the pyuria was greatly reduced, and function of the right kidney was improved. The nonfunctioning left kidney remained unchanged. This report is of interest in that it indicates a possible therapeutic approach to an extremely grave condition.

ANOMALIES OF THE ALIMENTARY TRACT

Congenital malformation of the alimentary tract was encountered five times in the 23 cases with necropsy reports and twice in patients still living at the time of publication of the reports. These 7 cases are briefly abstracted.

1. Blasi [11] in 1927 reported the case of a male infant 2½ months of age. The baby was a full term, normally delivered child. He was

10. Daut, R. V.; Emmett, J. L., and Kennedy, R. L. J.: Congenital Absence of Abdominal Muscles with Urologic Complications: Report on Patient Successfully Treated, Proc. Staff Meet., Mayo Clin. **22**:8, 1947.

11. Blasi, D.: Mancanza congenita bilaterale dei muscoli obbliqui dell' addome, Pediatria **35**:720, 1927.

brought under the author's observation because of two swellings at the lateral regions of the abdomen which were noted at the time of birth. The swellings were aggravated on crying. The baby had been constipated since birth. When examined, he weighed 3,700 Gm. and was thin and dehydrated. The most prominent sign was the great volume of the abdomen, which was shaped like a sack and presented two enormous lateral protrusions. This configuration of the abdomen contrasted with the narrowed thorax, which resembled the neck of a large vase. On the right, both the liver and the kidney were palpable; on the left, loops of small intestine were outlined under the skin. The spleen was palpable and not enlarged.

Obstipation and the discovery of an abnormally distended colon led to roentgenologic examination of the large intestine by means of a barium sulfate enema. This revealed an abnormal distention of all segments of the colon, especially the ascending and descending portions, which bulged into the lateral defect of the abdominal wall.

This patient had total absence of the two oblique muscles of the abdomen, with resultant protrusion of the ascending colon, the cecum and the liver on the right side and of the descending colon on the left. An elastic abdominal support was applied. The baby was doing well when last seen at 4 months of age.

2. Ikeda and Stoesser [12] presented the case of a 5 month old male infant. This child, the product of a normal full term gestation, was noted to have a toneless abdomen at birth, but he nursed well and gained weight satisfactorily. At 2 to 3 months of age, his thorax began to change its contour, the sternum protruding forward and upward. On physical examination, anterior protrusion of the thorax was observed to be prominent and a number of deep longitudinal furrows was seen in the abdominal wall. The umbilicus was represented by a linear scar about 1 cm. in length. All the visceral organs could be mapped out easily by palpation. The testes were undescended. Laboratory and roentgenologic findings were normal. Death was due to pneumonia. At necropsy the abdomen was asymmetric; the right half was distended because of the accumulation of loops of intestine. The subcutaneous tissue rested on the transversalis fascia, and there was no gross evidence of abdominal musculature throughout the entire abdominal wall. A dense fibrous band bound the umbilicus to the greatly hypertrophied urinary bladder. The bladder was considerably elevated above the symphysis pubis. The appendix hung free. The liver, spleen and gastrointestinal tract were otherwise normal. The left kidney weighed 35 Gm. The ureters were small with thick walls and narrow lumens. The wall of the bladder was

12. Ikeda, K., and Stoesser, A. V.: Congenital Defect in the Musculature of the Abdominal Wall: Case, Am. J. Dis. Child. 33:286 (Feb.) 1927.

contracted and diffusely thickened. The central nervous system was not examined. The apparent absence of a mesoappendix warrants inclusion of this case as one associated with a developmental anomaly of the gastrointestinal tract.

3. Moncrieff [13] described the case of a male infant 6 months of age, who died of pneumonia. He was the first child of healthy parents and was born at seven months' gestation by forceps delivery. He was noted to have a thin abdominal wall. The abdominal viscera were easily palpated. The bladder was felt as a lobular mass above the symphysis pubis. The surface of the abdomen was wrinkled with vertical linear markings. A slitlike umbilicus was present. The testes were undescended and the chest was deformed.

At necropsy, only a few strands of muscle fibers were seen in the upper part of the rectus sheaths and in other portions of the abdominal wall. The cecum had a mesentery and lay on the left side of the abdomen. The appendix was in front of the ileocecal junction. A large Meckel's diverticulum was present. The liver and spleen were normal. The genitourinary tract showed the greatest abnormality: The bladder was attached to the abdominal wall; the ureters were dilated and convoluted. Obstruction was encountered to passage of a probe into either ureter, but no obstruction was found in the urethra, nor was there any significant degree of phimosis. Both kidneys were enlarged, but without dilatation of the pelves. The testes were situated in the iliac fossae on each side, lateral to the ureters.

The abnormal position of the cecum in this case is explained on the basis of incomplete rotation of the midgut during fetal life.

4. Lichtenstein's [14] case was that of a white boy 3 years of age, who was admitted to Cook County Hospital, Chicago, for fever and cough of one week's duration. The large abdomen, which was noted at birth, had been unusually distended for four days, and difficulty in urination accompanied the distention. The most prominent observations consisted of pigeon breast deformity, protuberant abdomen and undescended testes. Roentgenologic examination of the lumbosacral portion of the spine showed no evidence of spina bifida. Excretory urography revealed dilatation of the right renal pelvis and calices, with dilatation and tortuosity of the ureter. The patient died of bronchopneumonia and peritonitis. When the abdominal wall was opened at necropsy, the abdominal muscles were absent; absence was confirmed by microscopic examination. The intestinal loops were matted

13. Moncrieff, A.: Specimens from a Case of Congenital Deficiency in Abdominal Muscles, Brit. J. Child. Dis. **28**:220, 1931.

14. Lichtenstein, B. W.: Congenital Absence of the Abdominal Musculature: Associated Changes in the Genitourinary Tract and in Spinal Cord, Am. J. Dis. Child. **58**:339 (Aug.) 1939.

together by loose green-gray membranes. The cecum and the vermiform appendix were observed near the midline below the left lobe of the liver. The cecum, appendix, ascending colon and ileum had a common mesentery which permitted free motility of these structures. The urinary bladder extended up to 7.5 cm. above the symphysis pubis. The kidneys weighed 210 Gm. The renal pelves were dilated. Both ureters were long, tortuous and dilated. Sections of the spinal cord showed no abnormalities of white or gray matter at various levels. In the anterior horns of the lower thoracic level the motor ganglion cells were slightly decreased in number and diminished in size. This change was attributed to so-called retrograde degeneration of the ganglion cells or atrophy of disuse.

In this case apparently there was a defect in intestinal rotation with failure of the cecum to descend to the right iliac region and of fixation of the mesentery to the posterior abdominal wall.

5. Eckhoff [15] described a 10 day old male baby who was admitted to the hospital because of hematuria on the third day of life and a large abdomen. Physical examination showed the abdomen to be obviously large and bulging in all directions. The abdominal wall was wrinkled and furrowed. The skin lacked elasticity and appeared to be stretched, though not actually thinned. Intestinal loops could be easily mapped out. The bladder was piriform and extended to the level of the umbilicus. Both kidneys were palpable. The testes were undescended. The chest was flattened from side to side, and Harrison's groove was present.

At necropsy the abdominal muscles were observed to be most deficient in the area adjacent to the urinary bladder. The viscera presented many unusual features. The bladder occupied a large part of the abdomen, extending upward for 2½ inches (6.4 cm.). A segment of colon lay transversely immediately above this, and the small intestine was visible at the sides. The right portion of the hypochondrium was occupied by the stomach, and the cecum and appendix were discovered immediately below this organ. The transverse segment of colon above the bladder was found to be the ascending colon, and the transverse colon lay doubled up behind this, terminating in the usual fashion. The bladder, ureters and renal pelves were enormously dilated. The genital organs were normal, except for cryptorchism.

This case is of particular interest because of multiple associated congenital anomalies, including deformity of the chest, genitourinary malformation, absence of the triangularis sterni muscle (this muscle is sometimes absent in normal persons) and the complicated malrotation of the gastrointestinal tract, including both the stomach and the midgut.

15. Eckhoff, N. L.: Congenital Deficiency of Abdominal Muscles, with Post-Mortem Report, Guy's Hosp. Rep. **73**:490, 1923.

6. In Stummer's [9] case the mesocecum was noted to be extremely long, indicating a lesser degree of malrotation.

7. Irvin and Kraus [16] described a 2 week old male baby with a lax abdominal wall noted at birth. A mass was palpable in the lower part of the abdomen, extending from the symphysis pubis to the umbilicus. The patient could never empty his bladder completely. A catheter was passed with difficulty; congenital urethral stricture was suspected. Therefore, a suprapubic cystotomy was performed. However, the patient died of bronchopneumonia three weeks after his admission to the hospital.

At necropsy, the gallbladder was disclosed to be in an abnormal position and the entire colon had a free mesentery similar to that of small intestine. The urethra was narrow but patent throughout. The bladder was extremely enlarged and hypertrophied, and also infected. Both ureteral openings were patent but narrow. The left ureter was extremely dilated and tortuous. The right ureter was less dilated. There was bilateral hydronephrosis with much reduction in renal parenchyma. The abdominal wall was thin and without musculature. Histologic study showed the ureteral wall to be made up chiefly of fibrous tissue, while the wall of the bladder had a well developed muscularis. The author was of the opinion that this observation indicated congenital hyperplasia of the ureter rather than compensatory hypertrophy due to organic obstruction. In this patient, as in the others, no clinical manifestations resulted from the error of intestinal rotation.

In these 7 cases, especially the third, fourth, fifth and seventh, the abnormalities of the abdominal parietes and of the genitourinary system were associated with manifest gastrointestinal anomaly due to errors in rotation. In no instance did malrotation give rise to clinical symptoms of intestinal obstruction. According to Dott,[17] 35 of 48 collected cases of anomalies of the second stage of rotation were accidental discoveries. He concluded that the incidence of asymptomatic cases must be much higher than has been appreciated. This fact probably explains the failure of previous authors to call attention to the presence of gastrointestinal anomaly in association with the more dramatic muscular and genitourinary deficiencies.

SUMMARY OF THE PUBLISHED CASES

Many of the individual case reports are too brief and incomplete to determine the nature or frequency of the several malformations associated with congenital maldevelopment of the abdominal muscles. The

16. Irvin, G. E., and Kraus, J. E.: Congenital Megaloureter and Hydroureter: Pathogenesis and Classification, Arch. Path. **45**:752 (June) 1948.

17. Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryology and Surgical Aspects, Brit. J. Surg. **11**:251, 1923.

available data, however, are assembled here and tabulated in table 1 to indicate the frequency with which various anomalies achieved recognition.

Number of Cases.—The total number of cases was 45. Fletcher's [6] case has been included in this tabulation because reference is made to it elsewhere in the literature, but it is pertinent to point out that the case was one of massive omphalocele and does not truly represent the malformation under discussion. Other reports are available, e.g., Gamble's [18] article, which describes large defects of the abdominal wall and evisceration. These are not included, as they apparently describe a totally different malformation probably involving other teratogenic mechanisms.

Sex.—There were 40 male and 2 female patients; the sex was not stated in three reports.

Age.—Twenty-seven of the patients died. Except for 1 patient who lived to the age of 3 years, all died in early infancy; 3 died at 1 year of age or under. Of the remaining 18 patients, 1 was alive at 70 years,[19] 1 at 60 years,[8a] 2 at 17 years,[20] 1 at 15 years,[21] 1 at 6 years,[8c] 1 at 3½ years,[19] 1 at 2 years [8d] and 8 at less than 1 year; in 2 the age was unstated at the time of the reports. The patient, still alive at 70 years, had a mild form of the malformation unassociated with an anomaly of the urinary tract; faradic stimulation of the abdominal muscles showed only partial absence of all the muscles. Henderson's report [8a] of the patient alive at 60 years was a brief one; apparently complications by other congenital malformations were lacking. The 2 patients still living at 17 years of age had associated anomalies of the urinary tract and were afflicted with recurrent episodes of urinary infection. Mollison's [23] patient was still living at 15 years of age, but because of much reduced vital capacity he was unable to take strenuous exercise and, owing to his inability to empty his bladder completely, he had recurrent attacks of cystitis. An abdominal binder was found to be effective as a support.

Causes of Death.—Eight patients died of pneumonia, 2 of uremia, 3 of diarrhea, 2 of "wasting" and 1 each of collapse and emphysema,

18. Gamble, H. A.: Congenital Absence of Part of the Abdominal Wall, South. M. J. **25**:771, 1932.

19. Hall, G.: Two Cases of Congenital Deficiency of the Muscles of the Abdominal Wall Associated with Pathological Changes in the Genito-Urinary Organs, Lancet **2**:1672, 1907.

20. Stumme.[8f] Gamble.[18]

21. Thatcher, L.: Case of Congenital Defect of Abdominal Muscles, with Anomaly of Urinary Apparatus, Edinburgh M. J. **11**:127, 1913.

22. Footnote deleted by author.

23. Mollison, W. M.: A Child with Absent Abdominal Muscles, Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) **2**:127, 1908-1909.

erysipelas, furunculosis and suppurative pericarditis, peritonitis, exfoliative dermatitis, septicemia, poor feeding and urinary infection. For 3 patients the cause of death was unstated.

Abdominal Muscles.—The rectus abdominis muscle was noted to be present, although deficient, in 25 cases. The segment above the navel was generally better developed than the lower segment. The obliquus externus abdominis was described in 14 instances, ranging from "trace" or "rudimentary" to "present." Similar descriptions of the obliquus internus abdominis muscle were encountered 11 times and of the transversus abdominis muscle 13 times.

Umbilicus.—The umbilicus was described as normal in 5 instances and as a slit in a longitudinal fissure or a linear central scar in 15 instances. It was normal in position in all the cases except that of Pels-Leusden,[24] in which the umbilicus was found to be 2 inches (5.1 cm.) above the midpoint between the symphysis and xiphoid process.

Thorax.—Pigeon breast deformity, narrowing of the thorax, anterior bulging of the sternum, flaring of the costal margins or Harrison's groove was noted in 20 cases. The thorax was described as normal in 2 cases and not mentioned in the remainder.

Testes.—Nondescent of the testes was the rule in these cases. Only in Fröhlich's report [4] was it stated that the testes were in the scrotum.[26]

Urinary Tract.—(*a*) Bladder: In 29 cases the bladder was hypertrophied and dilated. Five of these showed fixation of the bladder to the umbilicus. In 12 of the remaining 16 cases the condition of the bladder was not mentioned. Incomplete emptying of the bladder leading to cystitis was reported in Mollison's case [23] with a later follow-up study by Mackeith and his associates,[25] but it was said that roentgenologic examination of the urinary tract revealed nothing abnormal. The bladder was not palpable in 1 instance.[24] The urinary tract was said to be normal in the third case of Baxter's report.[2] Extreme contraction of the bladder was described in Hall's [19] second case. Of this group of 16 cases, in 11 the patient was still alive at the time of publication. Necropsy was performed in only 2 cases.[26]

(*b*) Ureters: The ureters were dilated in 20 cases. Howard [9] described dilatation in the upper part and atresia in the lower in both

24. Pels-Leusden, F.: Ueber den sogennanten congenitalen Defect der Bauchmusculatur, zugleich ein Beitrag zur Physiologie der Bauchmuskel- und Zwerchfellsfunction und zum Descensus testiculorum, Arch. f. klin. Chir. **85**:392, 1908.

25. Mackeith, N. W., and others: Observations on a Boy with Congenital Deficiency of the Anterior Abdominal Wall Muscles, Guy's Hosp. Rep. **73**:479, 1923.

26. Taillens, J.: Un cas d'agénésie des muscles abdominaux, Bull. Soc. de pédiat. de Paris **26**:277, 1928. Hall.[19]

his cases. Irvin and Kraus [16] described the ureters in their case as patent but narrow. The ureters were normal in Ikeda and Stoesser's case.[12]

(*c*) Kidneys: Hydronephrosis was observed in 10 cases; unilateral involvement of the right renal pelvis alone was reported in only 1 case.[21] The kidneys were palpable on physical examination in 3 cases. In 7 cases the kidneys were unequal in size. In 1 case the kidneys were not enlarged but were infected. Three cases showed cystic degeneration of the kidneys, unilateral or bilateral. In the case of Daut and his co-workers [10] the left kidney did not function.

(*d*) Urethra: Except for one of Howard's cases [9] in which there was atresia of the ureter and urethra, no true obstruction was found described in the other reports. Housden's report [8] of hypertrophy of the prostatic urethra causing obstruction was based on postmortem examination; the patient did not manifest symptoms of urinary obstruction during life. In Aldrich and Obrinsky's cases [27] a diverticulum of the urethra was seen at autopsy but caused no symptoms during life.

Gastrointestinal Tract.—Errors of rotation were encountered six times and magacolon once.

Other Congenital Malformations.—Deficiency of the quadratus lumborum muscle was noted in 4 cases; the latissimus dorsi was poorly developed in 1 instance. Deformity of the feet and legs was present in 6 cases. Another case was complicated by congenital dislocation of the hips. Spina bifida was observed once. Extreme retraction of the neck and head was recorded in another case.

II. REPORT OF CASES

CASE 1.—B. J. H.[28] was a full term white female baby born spontaneously Jan. 8, 1948 by cephalic presentation after a prolonged labor of ten hours. Both parents were healthy adults in their early thirties. The mother had periods of vomiting during the course of pregnancy but was otherwise well. The results of three previous pregnancies were (1) a boy born in 1942 who was living and well, (2) a full term baby who was hydrocephalic and died shortly after birth in 1944 and (3) a miscarriage in 1945.

The patient did not cry immediately after birth and required some manipulation before she started to breathe normally. Her face and hands were cyanotic. Shortly after birth, a normal-appearing meconium stool was passed. A few hours later repeated vomiting began, which in combination with a distended abdomen led to the provisional diagnosis of congenital megacolon. For this reason, the baby was referred to Dr. Paul Sutton and admitted to Children's Hospital for investigation and treatment.

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27. (*a*) Aldrich, C. A.: Report of a Case of Absence of Abdominal Muscles, Case Rep., Child. Memorial Hosp., Chicago **1**:13, 1942. (*b*) Obrinsky, W.: Agenesis of Abdominal Muscles with Associated Malformation of the Genitourinary Tract: A Clinical Syndrome, Am. J. Dis. Child. **77**:362 (March) 1949.

28. Dr. Paul Sutton gave us permission to publish this case report.

On her admission, the infant was 2 days old and weighed 5 pounds 11 ounces (2,580 Gm.). A slight degree of jaundice was present. The abdomen was large and soft. All parts of the abdominal wall were thin, and the lateral muscles were to all purposes absent. A wide diastasis recti was present. Both kidneys were palpable. Bowel patterns were easily seen across the upper abdominal wall. With the child recumbent, the flanks bulged and sagged like the abdomen of a pithed frog. The flaring costal margins made it possible to palpate the spleen. The heart and lungs and genitalia were normal.

Laboratory examination revealed a hemoglobin concentration of 19.9 Gm. and 5,000 white blood cells, with 57 per cent polymorphonuclear cells, 5 per cent

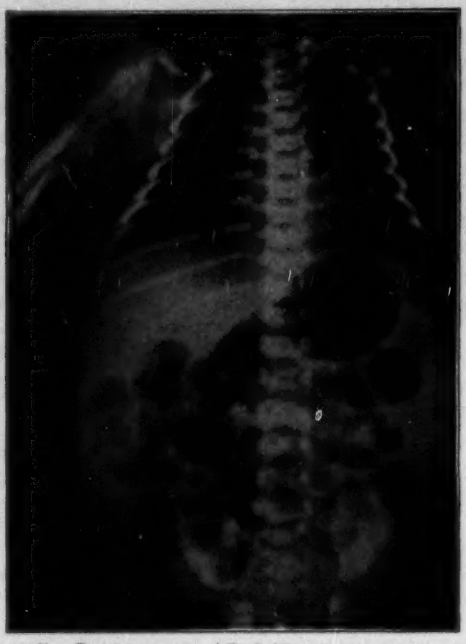

Fig. 1 (case 1).—Roentgenogram of B. J. H., a 2 day old white girl. The lax abdominal parietes is well demonstrated.

eosinophils, 34 per cent lymphocytes and 4 per cent monocytes. Urinalysis showed no abnormalities.

Roentgenologic examination of the abdomen revealed air-filled loops of bowel surrounded by a uniform water density consistent with free peritoneal fluid (fig. 1). Roentgenography with a barium sulfate enema demonstrated the cecum to be displaced anteriorly (fig. 2). This suggested either the presence of a retroperitoneal mass or incomplete rotation of the gastrointestinal tract with obstructive symptoms due to peritoneal adhesions.

After admission to the hospital, the patient vomited her feedings. She was given a blood transfusion, and a continuous intravenous infusion was begun. Operation

was performed on the day of admission. The rectus muscles were extremely thin. About 250 cc. of yellow fluid was found in the peritoneal cavity. The small bowel was twisted on its mesentery approximately 60 degrees in a clockwise direction. When the volvulus was corrected, the large bowel was easily identified and it was seen that the cecum and the ascending colon lay on the right side of the abdomen but high in the right upper quadrant. Thick bands attached the cecum and ascending colon to the posterior wall of the right upper quadrant and these appeared to obstruct the first and second portions of the duodenum. These bands were divided, and the cecum and ascending colon were elevated from the posterior abdominal wall and mobilized medially.

During operation, the operator carefully scrutinized the kidneys and thought that they were normal in appearance, as was the bladder. Dilatation of the ureters was not observed. The operative wound was closed in layers.

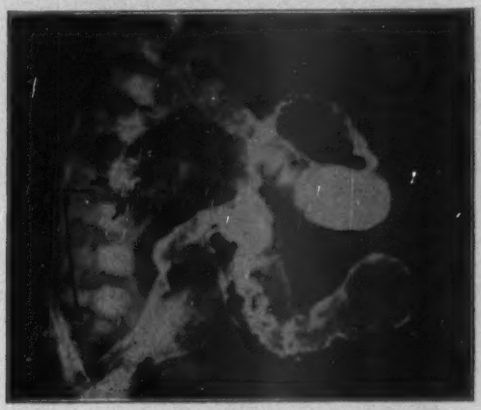

Fig. 2 (case 1).—Left posterior oblique projection during barium sulfate enema. Note anterior angulation of incompletely filled cecum which lies well above its normal position in the right lower quadrant.

After operation, the patient was maintained on intravenous alimentation for two days. Gradually, she was able to retain all feedings. She was discharged in good condition after two weeks of hospitalization.

The patient has been doing well ever since. She was last seen in August 1949, when she was 19 months old. She appeared to be active and bright. She weighed 23½ pounds (10.6 Kg.). Her height was 33 inches (83.8 cm.). There had been no further disturbance in the gastrointestinal or genitourinary tracts, and her development was apparently normal. She was able to sit up at 6 months and to walk at 1 year of age.

On physical examination at 19 months of age, her chest was observed to flare out at the lower border. The abdomen was flaccid and sagged when the child was erect; the walls bulged at both flanks in the recumbent position. The abdominal wall was smooth, and the umbilicus was well developed; with the child sitting, the skin of the abdominal wall was thrown into transverse folds (fig. 3). Abdominal reflexes were present on the right side but absent on the left. The liver and spleen

were palpable below their respective costal margins. The intestinal patterns were easily seen. The kidneys were not palpable, and the urinary bladder was not enlarged. The genitalia were normal. There was no gross evidence of deficiency of other muscles. No other associated anomaly was detectable.

This case presents two points of particular interest:

1. This is the only case of absence of abdominal muscles with an associated gastrointestinal abnormality alone, and the clinical picture of intestinal obstruction which appeared directly after birth was satisfactorily corrected by surgical treatment.

Fig. 3 (case 1).—Left, B. J. H. at 19 months of age erect. The intestinal pattern is seen through the thin abdominal walls. The surgical incision is well healed. Right, patient seated. The thin skin is thrown into transversely disposed folds. In the recumbent position, the flanks bulged laterad.

2. It is the third case reported to date of a female. In none of the 3 cases was there obvious involvement of the genitourinary tract. The inclusion of Fletcher's [6] case is probably most misleading here. Actually, ours is the second case reported in a female. Since genitourinary anomaly is so commonly associated with congenital absence of the abdominal muscles, one cannot be absolutely sure such an anomaly is not present without necropsy observation.

Case 2.—J. K., a full term white male infant, 4 days old, was admitted to Children's Hospital Aug. 30, 1949 because of a bulging and flaccid abdomen, which was noted at birth. The birth history was essentially normal. Both parents were healthy young adults. One sibling was living and well. The patient's uncle was said to have a defect of the left side of the face and to be mentally retarded.

Fig. 4 (case 2).—J. K., a 4 day old white boy in semirecumbent position. The thin abdominal walls bulge laterally. The intestinal pattern was more clearly defined than shown in the photograph.

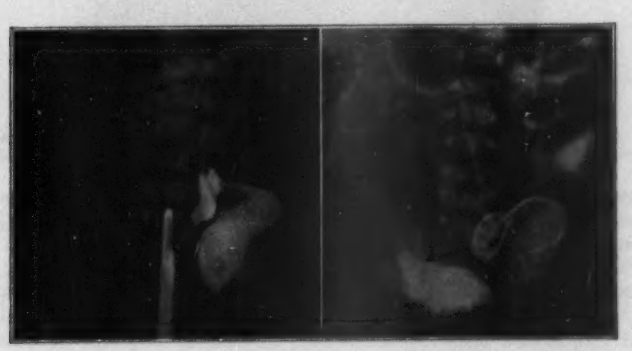

Fig. 5 (case 2).—Left, initial roentgenogram made after catheterization of left ureteral orifice and retrograde injection of dye. The catheter is coiled in the dilated, tortuous distal portion of the ureter. Right, roentgenogram taken after inversion of the infant. The degree of dilatation and elongation of the ureter is better demonstrated.

On physical examination, the patient was observed to be an active and vigorous baby weighing 8 pounds 6 ounces (3,799 Gm.). His color was good, and his respirations were regular. The rectal temperature was normal. The only positive signs were limited to the abdomen, which was conspicuously protuberant (fig. 4); the intestinal patterns were clearly visible through the bulging lateral walls. The umbilicus appeared normal in shape and position but was much shallower than usual. A few shallow vertical grooves were observed on the abdominal wall below the umbilicus. The rectus muscles above the navel seemed to be present; a thick cordlike structure (ligamentum teres?) was felt in the hypochondriac region extending upward from the umbilicus. The liver and spleen were palpable. The

Fig. 6 (case 2).—Cystogram in lateral projection. The bladder is dilated and follows the contour of the anterior abdominal wall. Some ureteral reflux is present.

kidneys were not enlarged. At no time was the bladder palpable. The testes were undescended, but the scrotum was well developed. The thorax and extremities were normal.

After his admission, the patient's general condition continued good, and he was afebrile. The feedings were well tolerated and passage of stool was normal.

Laboratory Studies.—Laboratory examination showed 20.4 Gm. of hemoglobin per hundred cubic centimeters of blood and 6,200,000 red blood cells and 15,550 white blood cells per cubic millimeter. The differential count was normal. Urinalysis showed a trace of albumin and a few white and red cells in the sediment. Nonprotein nitrogen was determined three times preoperatively as 36, 44 and 54 mg. per hundred cubic centimeters, respectively.

Roentgenologic Studies.—Excretory urographic study on September 7 resulted in nonvisualization of both kidneys; the lumbosacral portion of the spine was normal. The procedure was repeated on September 13, with demonstration of bilateral hydronephrosis.

A cystoscopic examination on September 17 showed an essentially normal bladder, except for some slight shifting of the trigone to the right. The catheter could enter the right ureteral orifice for a distance of ¼ to ½ inch (0.6 to 1.3 cm.), but not beyond because of folding of the bladder wall. The left ureteral orifice was catheterized relatively easily. Roentgenograms taken after the introduction of the contrast medium showed a greatly dilated and tortuous left ureter (fig. 5).

Fig. 7 (case 2).—Postoperative cystogram. Reflux has occurred on the right only. The ureterectasis is not appreciably changed.

Although examination was not successful on the right side, it was believed that the process was a bilateral one.

A cystogram taken on September 30 showed that the bladder was attached to the anterior abdominal wall (fig. 6). A series of films, including a voiding urethrogram, failed to demonstrate the existence of urethral obstruction.

In view of the rather frequent association of gastrointestinal anomaly with congenital absence of the abdominal muscles, roentgenography with a barium sulfate enema was performed; this revealed a freely movable cecum and ascending colon. The cecum could be moved to the midline at the level of the transverse colon and then back to its normal position.

Course in the Hospital.—On September 26 the patient's temperature went up suddenly to 104 F., and urinalysis showed a 4 plus reaction for albumin and

numerous white and red cells. Subsequently there were several episodes of this kind, all controlled by chemotherapy. The urine was cultured repeatedly; several organisms were obtained on different occasions, including Aerobacter aerogenes, Escherichia coli, Proteus morganii, nonhemolytic Staphylococcus albus and Alcaligenes marshalli. Nevertheless, the patient's general condition remained excellent.

An exploratory laparotomy was performed on October 12. No definite muscle fibers were observed when the abdomen was entered by a midline suprapubic incision. The bladder was large and flabby; the ureters were redundant, tortuous

Fig. 8 (case 3).—Roentgenogram showing lax abdominal walls as indicated by the bulging flanks (photograph furnished by Dr. Charles Buchert).

and dilated to the size of a man's thumb. Near the bladder the ureters narrowed to a more normal caliber for a distance of about 1 cm. When the bladder was opened, inspection revealed no evidence of trabeculation; the vesical neck appeared normal, and no obstruction could be identified. The ureters were divided close to the bladder and reimplanted on each side near the dome through stab incisions. A suprapubic drain was left in the bladder.

At the last examination, two months after surgical intervention, the child was eating and gaining well but had persistent pyuria and bacilluria despite intensive antibiotic therapy. The suprapubic wound was just healing over, and the baby was voiding well by the urethra. Cystograms had shown reflux into the right ureter

but none on the left side (fig. 7), and the nonprotein nitrogen content of the blood remained in the normal range. The ultimate prognosis remains guarded but would be improved by control of the urinary infection.

CASE 3.[29]—A full term white male infant, weighing 7 pounds (3,175 Gm.), was born on Aug. 13, 1949 at the Middletown Hospital, Middletown, Ohio. When the infant was first seen by Dr. Charles Buchert, an extremely thin abdominal wall was noted and two cystic masses were palpable in both lower quadrants. Both testes were undescended. Respiration and color were good. The child did well and gained weight on formula feedings. However, the masses seemed to increase in size. A roentgenogram of the abdomen (fig. 8) showed a diffuse soft tissue density posteriorly which displaced the gas pattern of the intestine anteriorly. Roentgenologic study by means of a barium sulfate enema revealed a normal large intestine

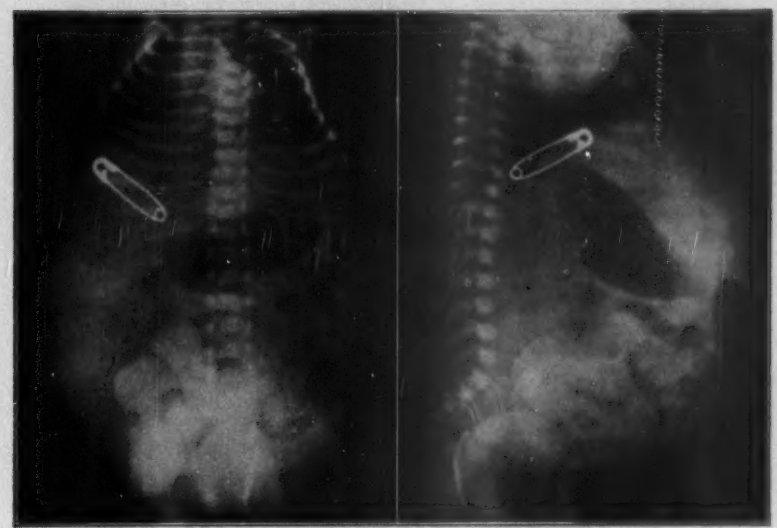

Fig. 9 (case 3).—Left, cystogram in anteroposterior projection. The right ureter has filled and is tremendously dilated and elongated. Right, cystogram in lateral projection. (Photographs furnished by Dr. Charles Buchert.)

and displacement of the large and small intestine anteriorly and upward. Excretory urography was unsatisfactory. Laboratory studies revealed 10,000 white blood cells per cubic millimeter, with a normal differential count, a hemoglobin concentration of 17 Gm. and 5,000,000 red blood cells per cubic millimeter. The Kahn reaction was negative. A huge dilated right ureter was observed on cystography; no dye was seen to enter the left ureter (fig. 9).

On August 20 an exploratory laparotomy was performed. The left ureter was found to be a large cystic structure measuring 10 to 14 inches (25 to 36 cm.) in length and to be folded back on itself twice. A long segment was resected and an anastomosis was performed between the remaining ureter and the renal pelvis. The

29. Dr. Charles Buchert, Middletown, Ohio, has permitted us to report this case.

kidney was palpated on both sides and noted to be normal. The child withstood the operation well, and the postoperative course was initially uneventful. Postoperatively, the patient received penicillin, sulfadiazine and streptomycin. However, on the fourth postoperative day, the temperature began to rise and signs of pneumonia were detected in the right lung. At the same time, another large cystic mass was palpated in the right lower quadrant. This enlarged rapidly and definitely interfered with the patient's respiration. The patient died on the ninth day in the hospital.

At autopsy (performed by Dr. R. C. Dunn) the body appeared normal in development except that the testes were not descended. The cecum was a few inches short of being completely rotated, but the other organs were in their normal location. Both kidneys appeared enlarged and soft due to dilated pelves. The parenchyma was thin. The right ureter was dilated, tortuous and elongated. The left was dilated, short and sutured at the lower end. The ureters and the urethra were patent. Atrophic testes were observed in the peritoneal cavity.

Microscopic examination showed severe hypertrophy of the wall of the bladder, but the mucosa was unchanged. The kidneys showed some atrophy of the cortex of both sides, with evidence of infection on the left. The prostatic urethra appeared normal.

The pathologic changes in the urinary tract of this patient are similar to those noted in case 2. Both patients demonstrated normal bladder mucosa; thus, it is unlikely that obstruction of the lower part of the urinary tract is responsible for the anomalous position of the cecum. The gastrointestinal malformation was asymptomatic in this patient.

III. COMMENT

PATHOGENESIS

Absence or even hypoplasia of the abdominal muscles may be expected to affect other body systems by virtue of the functional relationship of the muscles to the particular system. Maintenance of intra-abdominal pressure is effected by the abdominal muscles, assisted by the diaphragm and the thoracic muscles. Intra-abdominal pressure influences intestinal peristalsis and assists in the processes of defecation and micturition as well as others not pertinent to the discussion. Therefore, in congenital absence of the abdominal muscles incomplete emptying of the bladder leading to urinary retention and infection is to be expected. Constipation and symptoms of indigestion are common complications.

Moreover, the domelike contour of the diaphragm and the cylindric shape of the chest are maintained by these muscles. Deficiency makes necessary a thoracic type of respiration, and the diaphragm is flattened. Deformity, therefore, easily develops in the yielding infantile thoracic cage. The frequency of these associated manifestations has been alluded to in the summary of the published cases.

Muscular Anomalies.—The pathogenesis of the common malformations in this group of cases has been discussed at great length in the literature. The various theories are summarized as follows:

1. Primary Developmental Defect of the Abdominal Muscles: Scammon (Ikeda and Stoesser [12]) was of the opinion that the abdominal condition is due to an embryonic arrest of the development of the abdominal muscles which failed to extend forward to the anterior abdominal wall.

The somites from which the muscles originate first develop in embryos of about 1 to 2 mm. and increase in number until there are 38 to 41 pairs. The somites undergo differentiation to form the myotome, or muscle plate. The superficial portions of the myotomes lose their segmental character quickly and fuse to form a longitudinal myotomic column from which the deep muscles of the neck and back are formed. The ventrolateral divisions of the myotomes of the first thoracic to the first lumbar somites give rise to the anterior and lateral muscles of the thoracic and abdominal walls. The intercostal, oblique and transversus muscles originate from the main lateral sheet, while the ventral edge forms the rectus muscles.

If the lower portion of the myotomic column fails to grow anteriorly or if it grows incompletely, absence or partial development of the abdominal muscles will result.

Batten made a careful study of the abdominal wall of Garrod and Davies' patient [31] and compared it with a specimen from a normal child of the same age. The total thickness of the abdominal wall from the skin surface to the peritoneum was the same for the patient as in the normal specimen. In the patient, more than two thirds of the entire thickness of the abdominal wall was in the form of epidermis, cutis and subcutaneous tissue. The muscular layer formed less than one third of the total thickness of the abdominal wall. The proportions were reversed in the normal specimen. On microscopic examination, the muscle fibers from the patient's abdomen did not resemble normal muscle fibers in shape and striations. The fibers of the aponeurosis were completely absent in sections of the abdominal muscles. Batten concluded that these muscle fibers resembled unstriped muscle fibers or fibers in the early stage of development. Nothing suggested atrophy of a normally developed muscle.

Lichtenstein [14] was also of the opinion that a primary developmental defect is involved. He stated:

> From the histologic study of the abdominal wall . . . the complete absence of the abdominal musculature without traces of either a connective tissue scar or atrophic or dystrophic muscle fiber speaks rather for congenital absence than for pressure atrophy or fetal muscular dystrophy.

30. Footnote deleted.

31. Garrod, A. E., and Davies, L. W.: On a Group of Associated Congenital Malformations, Including Almost Complete Absence of the Muscles of the Abdominal Wall, and Abnormalities of the Genito-Urinary Apparatus, Med.-Chir. Tr. **88**:363, 1905.

2. Primary Genitourinary Malformation; Secondary Changes in Abdominal Muscles: The frequent association of hypertrophy and dilatation of the bladder with congenital absence of the abdominal muscles has led others to state their belief that the defect of the abdominal muscles is secondary to the pressure effect of the greatly hypertrophied and dilated bladder. It was thought that atrophy of the rectus muscle is due to the direct effect of the enlargement of the bladder, while that of the obliquus and transversus muscles is due to the pressure effect of the much dilated ureters. Some writers have even advanced the theory that

TABLE 2.—*Embryologic Development of the Gastrointestinal and Genitourinary Tracts and the Muscular System* *

Age, Wk.	Size, Mm.	Digestive Tube and Glands	Urogenital System	Muscular System
3	1.5	Gut not distinct from yolk sac	Allantois present	.....
4	2.5	Foregut and hindgut present; yolk sac broadly attached at midgut; liver bud present	All pronephric tubules formed; pronephric duct growing caudad as a blind tube	Mesodermal segments appearing; older segments show myotome plates
5	5.5	Esophagus short; stomach spindle shaped; intestine a simple tube; liver cords, ducts and gallbladder forming	Pronephros degenerated; pronephric duct reaches cloaca; Mesonephric tubules forming	All mesodermal segments present
6	11.0	Yolk sac detaches from gut; stomach rotating; intestine elongated into loops which undergo torsion; cecum becomes prominent	Secretory and excretory primordia of metanephros evident; sexless gonad and genital tubercle prominent; müllerian ducts appear; urogenital sinus separating from rectum	Myotomes fuse into a continuous column and spread ventrad
7	17.0	Stomach attaining final shape; duodenum temporarily occluded; intestinal loops herniate into cord	Metanephric collecting tubules begin branching; earliest metanephric secretory tubules differentiating; urethral membrane ruptures	Muscles differentiating rapidly and assuming final shapes and proportions
9	35.0	Small intestine coiling within cord; intestinal villi developing; appendix indicated	Bladder distinct from urethra	Definitive muscles of trunk, limbs and head well represented and fetus capable of some movement
10	43.0	Intestine withdraws from cord and assumes characteristic positions; anal membrane ruptures	Union of mesonephric and testicular tubules to complete male duct; male or female duct degenerating in opposite sex	Perineal muscles developing tardily

* Table modified from Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1935, table opposite p. 194.

ventral bulging of the bladder may prevent the formation of the abdominal muscles. This concept is untenable because the abdominal muscles are formed by the end of the ninth week (table 2), long before pressure can be exerted on them by distention of the urinary bladder. Housden [6] was of the view that secondary atrophy of muscles already formed by pressure of the dilated bladder is more probable. His explanation was supported by the following observations:

(*a*) The presence of wrinkles and furrows on the surface of the abdominal wall in most cases suggests the possibility of a period of great distention by pressure from within.

(*b*) In most cases only the lower segment of the rectus was deficient, which speaks in favor of pressure in that region.

However, there are many instances of congenital hydronephrosis, hydroureter and hypertrophied bladder in which no abnormalities are detected in the abdominal muscles. Furthermore, there are a few cases of congenital absence of the abdominal muscles not associated with dilatation of the bladder.

3. Primary Muscular Defect and Secondary Changes in the Genitourinary System: Bardeen (Osler [20]) stated that owing to the lack of resistance in the abdominal wall normally met with by the urinary bladder it expands rather than contracts. Normally, micturition is effected by the combined forces of contraction of the detrusor muscle of the urinary bladder and contraction of the abdominal muscles and the diaphragm. A similar mechanism is believed to exist in intrauterine life. Thus, the lack of the accessory force from the abdominal muscles permits accumulation of urine in the bladder which becomes dilated and hypertrophied, and, secondarily, hydronephrosis and hydroureter occur. These mechanisms might explain the cases with dilatation and hypertrophy of the urinary bladder as the only change in the urinary tract, there being no dilatation of the ureters or the renal pelves.

Bardeen also expressed his belief that an abnormal arrangement of the blood supply to the abdominal muscles may impede their development, and a similar vascular disturbance may account for the changes in the genitourinary tract. The vascular plexus for the abdominal wall is formed above by the internal mammary artery and below by the epigastric artery. However, the result of Batten's microscopic study of Garrod and Davies' patient did not support this belief. Batten stated that the general appearance of the muscle cells did not suggest a vascular origin for the malformation.

4. Intrauterine Poliomyelitis: Intrauterine poliomyelitis has been suggested as the cause of atrophy of the abdominal muscles. Batten examined the spinal cord of Garrod and Davies' patient and found it was grossly normal. On section at various levels the diameter was equal to that of a normal cord from a child of the same age. The number of cells in the anterior horns of five consecutive sections at each level of the thoracic region was counted and compared with a similar count in a normal child. No significant alteration was discovered, and Batten concluded that there was no basis for the implication of poliomyelitis as a causal factor.

The result of Lichtenstein's [14] study of the spinal cord of his patient and Hall's report [19] on the study of the spinal cords of his 2 patients also speak against such an explanation.

5. Congenital Syphilis: Brindeau and Jacquet in 1928 [32] reported a case of congenital absence of the abdominal muscles in a newborn baby who had an ulcer of the umbilicus due to congenital syphilis. There is no support for the belief that syphilis was other than an incidental feature.

Genitourinary Anomalies.—The pathogenesis of the associated genitourinary anomaly likewise has been discussed extensively in the literature, both in relation to the muscular defects and independently.

1. Guthrie [8c] in 1896 suggested that the firm attachment of the bladder to the anterior abdominal wall prevents it from contracting and emptying itself. As the result of contracting against such a great resistance, the wall of the bladder becomes dilated and hypertrophied. However, the bladder was not adherent to the anterior abdominal wall in all cases.

2. Vascular disturbance or lack of abdominal muscles as the cause of dilatation and hypertrophy of the bladder has been discussed previously.

3. Much speculation has arisen with regard to obstruction of the lower part of the urinary tract as the cause of dilatation and hypertrophy of the bladder.

Stumme [8f] first suggested that obstruction of the urethra at a comparatively late period of embryonic life causes retention of urine and dilatation and hypertrophy of the bladder and ureters. He stated his belief that the cause of urinary retention disappeared later. In his case he presumed that the attachment of the urinary bladder to the anterior abdominal wall altered the anatomic relationship of the urethral and ureteral orifices, thereby producing obstruction of the intramural portion of the ureters and of the vesical orifice of the urethra. However, this explanation does not apply to the cases without fixation of the urinary bladder to the anterior abdominal wall. Definite mechanical obstruction of the lower part of the urinary tract was advocated by Housden,[8] but no evidence of obstruction to urinary outflow was observed during life in his patient. Daut and his co-workers [10] of the Mayo Clinic performed a transurethral resection of the vesical neck in their patient, with decided improvement of the clinical condition.

On the other hand, Irvin and Kraus [16] considered their patient to have megaloureter as a result of congenital hyperplasia without evidence of organic obstruction. They cited the embryologic studies of Gerard which indicated that the ureteral bud is large in relation to other portions

32. Brindeau, A., and Jacquet, E.: Agénésie des muscles abdominaux chez un nouveau-né hérédo-syphilitique, Bull. Soc. d'obst. et de gynéc. **17**:826, 1928.

of the urinary tract up to the fifth month of fetal life. Therefore, a large hypertrophied ureter was thought to represent a lack of the inhibition of ureteral growth which normally occurs after the fifth month. In Howard's [9] patient, the presence of congenital atresia of both ureters makes it difficult to explain the hypertrophy of the bladder on the basis of obstruction of the lower part of the urinary tract, unless one can accept the possibility that the atresia of the ureters is secondary to pressure by the enlarged bladder. Some cases may show evidence of obstruction while others do not. Therefore, a single etiologic factor may not suffice to explain all the cases.

In our cases 2 and 3, the bladder mucosa was observed to be normal without increase of trabeculation, a circumstance which makes unlikely the presence of an organic obstruction in the lower part of the urinary tract. This type of case has been considered to be of neurogenic origin, analogous to Hirschsprung's disease in its pathogenesis. However, further study must be carried out to confirm this supposition. In this respect, Blasi's [11] case is of interest since megacolon was present. Earlier studies were concerned with the number of cells in the spinal cord; the recent emphasis on deficiencies of intramural nervous plexes in Hirschsprung's disease [33] warrants careful study for similar changes in megaloureter.

Nondescent of the testes is the rule in all these cases. The cryptorchism is best explained on the basis of mechanical obstruction of the inguinal canal by the enormous bladder and ureters.

Gastrointestinal Anomalies.—In the cases associated with gastrointestinal anomaly, it is impossible to say whether there is any interrelationship between the development of the intestine and that of the abdominal muscles. Dott [17] stated his belief that variation in size of the embryonic umbilical orifice is the most probable cause of anomalies of intestinal rotation. Normally, during the second stage of rotation, the prearterial segment of the small intestine becomes elongated first and reenters the abdomen on the right side of the superior mesenteric vessels, passing to the left side of the abdomen behind these vessels. The cecum then enters the abdomen and is generally fixed in the right upper quadrant. As the ascending colon gradually elongates and the liver

33. Zuelzer, W. W., and Wilson, J. L.: Functional Intestinal Obstruction on a Congenital Neurogenic Basis in Infancy, Am. J. Dis. Child. **75**:40 (Jan.) 1948. Bodian, M.; Stephens, F. D., and Ward, B. C. H.: Hirschsprung's Disease and Idiopathic Megacolon, Lancet **1**:6, 1949. Swenson, O., and Bill, A. A., Jr.: Resection of Rectum and Rectosigmoid with Preservation of the Sphincter for Benign Spastic Lesions Producing Megacolon: An Experimental Study, Surgery **24**:212, 1948.

ascends, the cecum becomes situated in the right lower quadrant. According to Dott, if the embryonic umbilical orifice is too large, both the small intestine and the cecum can be reduced with equal facility and the competition may give rise to a disorderly sequence of return of the midgut loop. In studying the embryology of the abdominal muscles, Frazer (Housden [8]) showed that the three muscles of the lateral abdominal wall are distinguishable at the end of the fifth or beginning of the sixth week of fetal life. By the time the gut in the umbilical sac is ready to withdraw into the abdomen at the end of the ninth week, the two recti constrict the opening of the sac and close it quickly on the withdrawal of the gut. If the recti muscles are deficient, it is conceivable that the sac retains an abormally enlarged orifice, thus the process of intestinal rotation may proceed in an abnormal fashion. If this explanation is valid, the malrotation of the intestine could be secondary to the deficiency of the abdominal muscles. However, one cannot overlook the possibility of independent occurrence of these various anomalies.

The fact that our 3 patients demonstrated anomalies of midgut rotation, and that 6 other patients in the literature presented varying degrees of the same malformation, indicates that this is probably an occurrence of considerable frequency. A total of 9 patients among 26 examined, 24 by necropsy and 2 by roentgenography, with findings confirmed at surgical intervention, is of significance, since many of the necropsy reports were incomplete with respect to the condition of the alimentary tract.

Apart from indicating another component in a rare clinical syndrome, the observation may be of value in its teratologic implications. In table 2 data concerning the development of the alimentary tract, the urogenital system and the muscular system are arranged in simultaneous chronologic order. During the sixth and seventh weeks, the muscular and urogenital systems are in the stage of development which if arrested or altered could produce the malformations described. The process of midgut rotation takes place during the fifth to the tenth weeks. A disturbance of embryogenesis which is to result in malformation in all three systems must occur before the tenth week of fetal life, and probably before the eighth week. The earliest limit cannot be defined, since acquired aberrations of chromosomes may occur up to the time of oogenesis and spermatogenesis.

PROGNOSIS

Congenital absence of the abdominal muscles carries a serious prognosis because of the great frequency of associated genitourinary anomalies. However, the patient with a mild malformation unassociated with other abnormalities usually can lead a normal life.

TREATMENT

The use of mechanical devices to support the abdominal wall should be emphasized in all cases. Abdominal support in the form of an elastic bandage or a nonelastic corset will serve to protect the abdominal viscera from injury, to substitute in part for the absent muscles and to facilitate walking and creeping in infancy.

General supportive measures in the form of nutritional care and prevention of infection are important in eliminating complications.

Early surgical intervention is indicated in patients with symptoms of intestinal obstruction due to an associated anomaly of the gastrointestinal tract.

The abnormality of the genitourinary tract should be explored early in life for the performance of possible reparative procedures, such as separation of an adhesive band between the umbilicus and the anterior abdominal wall, resection of redundant ureters and relief of ureterovesical obstruction. If there is any suspicion of the presence of mechanical obstruction in the lower portion of the urinary tract, surgical intervention should be contemplated as soon as possible.

SUMMARY AND CONCLUSIONS

The literature on congenital absence of the abdominal muscles associated with anomalies of the genitourinary tract is reviewed, and the various theories with regard to the pathogenesis of this syndrome are briefly summarized.

Three cases of congenital absence of the abdominal muscles are described. The first was of a female child 19 months of age, who was first seen for symptoms of intestinal obstruction manifested shortly after birth, due to malrotation of the gastrointestinal tract. She was successfully treated surgically. During the operation, the genitourinary tract was carefully examined, and no evidence of malformation was found. She is leading a normal and active life at present.

The second patient was a male newborn infant with bilateral hydronephrosis, hydroureter and dilatation of the bladder. The condition was improved by resection of the tortuous and redundant ureters and their transplantation to a higher position in the bladder. This patient also had roentgenologic evidence of malrotation of the gut and bilateral cryptorchism.

The third patient was a male newborn child with congenital hydroureter and hypertrophy of the bladder. On exploratory laparotomy, the dilated left ureter was partially resected and the remnants were anastomosed. The patient died of pneumonia shortly after the operation. Necropsy revealed malrotation of the large bowel in addition to the anomaly of the urinary tract.

Attention is directed to malformations of the gastrointestinal tract, particularly malrotation, as a previously unrecognized component of the syndrome. Of 24 cases in the literature with autopsy, there were 5 instances with evidence of malrotation of the gut. One patient, still alive at the time of publication, had a noticeably long mesocecum, and another had an associated congenital megacolon. The addition of our 3 cases to the 6 with malrotation of any degree provides a total of 9 cases among 48 reported of congenital absence of abdominal muscles. The incidence of anomaly of the alimentary tract is, therefore, at least 20 per cent. This is sufficiently high to warrant investigation of the gastrointestinal tract in all future cases.

The relationship of malrotation of the gut to congenital absence of the abdominal muscles is discussed briefly.

Elland and Bethesda Avenues.

News and Comment

ANNOUNCEMENTS

Grants for Pediatric Research.—Twelve research projects in pediatrics will be supported this year through grants from the newly organized Playtex Park Research Institute, it was announced early this month by the Board of Governors through the Executive Committee, Drs. Sidney Farber, Charles F. McKhann and Joseph Stokes and Mr. Walter O. Heinze. The twelve grants are the first made by the Institute, which was established in September 1949 by the International Latex Corporation. With one exception, all grants will be supported for a period of three years beginning July 1, 1950. A list of the projects follows:

Ephraim Shorr, M.D., New York Hospital–Cornell University Medical College, Growth Defects in Children, three years.

Bret Ratner, M.D., New York Medical College–Flower and Fifth Avenue Hospital, The Passage of Proteins Through Living Membranes, three years.

Charles F. McKhann, M.D., Western Reserve University, Babies Hospital, Cleveland, Increasing Blood Supply to the Brains of Mentally Retarded Children, three years.

Samuel Z. Levine, M.D., New York Hospital–Cornell University Medical College, The Relation of Adrenal Hormones to Aromatic Amino Acid Metabolism in Premature Infants, three years.

E. Stewart Taylor, M.D., and Paul D. Bruns, M.D., University of Colorado, Study of Uterine Contraction Throughout Pregnancy with Particular Reference to Uterine Motility in Pregnancies Which Come to Term and Those Which End Prematurely, three years.

Nathan B. Talbot, M.D., Massachusetts General Hospital, Boston, Physiology of Endocrine Abnormalities, three years.

Myron E. Wegman, M.D., Louisiana State University School of Medicine, Adrenal Hormones and Infections, three years.

James L. Wilson, M.D., University of Michigan, Physiologic Basis of Diarrhea in Infancy, three years.

Charles C. Chapple, M.D., Children's Hospital of Philadelphia, Growth-Promoting Factors Related to Kidney Function, three years.

Milton J. E. Senn, M.D., Yale University Child Study Center, The Role of Emotional Factors in the Causation, Precipitation and Perpetuation of Disease, three years.

Jonathan Cohen, M.D., Harvard Medical School, Boston, The Identification of Factors Concerned with the Growth of Bone, three years.

Richard L. Day, M.D., Babies Hospital, College of Physicians and Surgeons, Columbia University, Hormone Factors in Premature Infant Metabolism, one year.

Interested investigators are invited to communicate with the Playtex Park Research Institute, P. O. Box 244, New York 19. Application forms for grants will be mailed on request.

American Board of Pediatrics, Inc.—Following are the schedules for oral examinations to be held by the American Board of Pediatrics, Inc.:

Chicago, October 13, 14 and 15, 1950

Boston, December 1, 2 and 3

Written examinations have already been held.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

THE EFFECT, IN RATS, OF HIGH FAT DIETS ON THE RENAL EXCRETION OF WATER AND ANTIDIURETIC SUBSTANCES. STEPHEN H. LESLIE and ELAINE P. RALLI, Endocrinology **41**:1 (July) 1947.

The rate of urinary excretion was altered in rats fed a high fat, low protein diet, the onset of diuresis being delayed and the total amount lessened. Urines of the rats on the high fat diet, with or without sodium chloride, when extracted and injected into hydrated normal rats, were observed to exert a definite antidiuretic effect.

JACOBSEN, Buffalo.

MEAT IN THE DIET OF YOUNG INFANTS. RUTH M. LEVERTON and GEORGE CLARK, J. A. M. A. **134**:1215 (Aug. 9) 1947.

No adverse symptoms occurred when the protein intake of 18 bottle-fed infants was increased 25 per cent by the addition of approximately 1 ounce (28 Gm.) of strained meat (veal, beef, pork and lamb) to the formula when the infants were 6 weeks old. The general well-being of these infants seemed better than that of the 15 controls. The average hemoglobin levels before the experiment were for the group given meat, 10.5 Gm. and, for the controls, 10.7 Gm. per hundred cubic centimeters. After the eight week period of meat feeding the levels were, respectively, 11.9 Gm. and 9.6 Gm. per hundred cubic centimeters, suggesting that the meat feeding not only checked the drop in hemoglobin level characteristic of children of this age but promoted hemoglobin formation.

BAIRD, Wauwatosa, Wis.

THE MECHANISM OF AMPHETAMINE-INDUCED LOSS OF WEIGHT: A CONSIDERATION OF THE THEORY OF HUNGER AND APPETITE. STANLEY C. HARRIS, A. C. IVY and LAUREEN M. SEARLE, J. A. M. A. **134**:1468 (Aug. 23) 1947.

It was demonstrated by controlled experiments on human and canine subjects that the administration of amphetamine sulfate may cause or facilitate a loss of body weight in obese and nonobese persons. The evidence shows that the loss of weight observed in these experiments was due primarily to a reduction in the intake of food.

In a group of 10 subjects who maintained a constant caloric intake for one hundred days the administration of amphetamine sulfate for fifty-six days caused some loss of weight during the first four to eight days in 7 of the subjects. This loss of weight was most reasonably attributed to a slight (approximately 10 per cent) increase in energy metabolism due to restlessness, which disappeared on the development of tolerance. No evidence of deleterious effects of the drug was observed.

A daily dose of 5 to 10 mg. of amphetamine sulfate injected subcutaneously into dogs (8 to 10 Kg. of body weight) one hour before the presentation of food, which was left in the cage for forty-five minutes, caused a complete abolition of food intake for from ten to twenty-one days in some dogs. This action of the drug was not influenced by extrinsic denervation of the stomach and intestine. The evidence was interpreted as an indication that the drug produces anorexia by acting on an appetite mechanism in the cerebrum or on a hunger mechanism resident at a lower

level (hypothalamus) or on both. Means for testing the validity of this interpretation are suggested.

FROM THE AUTHORS' SUMMARY.

A SELF-REGULATING FEEDING PROGRAM FOR INFANTS. C. ANDERSON ALDRICH and EDITH S. HEWITT, J. A. M. A. **135**:340 (Oct. 11) 1947.

This is a report on the feeding of 668 babies during their first year by the self-regulating method, a term preferred to the "self-demand method."

During the neonatal period the babies were cared for in the typical hospital nursery and fed on a four hour schedule, unless they showed a distinct need for more frequent feedings. On discharge the mothers were told to feed the babies all they wanted whenever they were hungry. Follow-up monthly clinic visits continued this program. Mothers were given leaflets telling them what to expect at each monthly age. The type of food which may be given was prescribed, but the times of feeding and the amount and variety of foods were not given.

One hundred infants were studied intensively during the year to determine the rhythm of change from early feedings (irregular or every two, three or four hours) to the three or four meal a day schedule at 1 year of age. Only 26 per cent of the babies were ready for a four hour schedule at 1 month of age. Ninety-one per cent were on a three meal a day schedule at the age of 1 year. At 1 year of age 92 per cent of the babies had excellent appetites. Their heights and weights compared favorably with the accepted standards.

BAIRD, Wauwatosa, Wis.

THE ADVISABILITY OF BREAST FEEDING: A SURVEY OF THE SUBCOMMITTEE OF THE COMMITTEE ON MATERNAL AND CHILD FEEDING, NATIONAL RESEARCH COUNCIL. C. ANDERSON ALDRICH, J. A. M. A. **135**:915 (Dec. 6) 1947.

As a food, human milk still remains the best type of milk for young infants, although it probably is not always a complete food after the first few weeks. Breast milk has definite preventive and therapeutic value. It is economical, automatically produced and timesaving in the household. By and large, the country over, breast milk is the safest food for premature babies who are mature enough to suckle at the breast. The younger ones may need special nutritional and other facilities.

As a technic, breast feeding probably is the best method of providing gratification and a sense of security to babies. However, even when she is using artificial feeding, the loving mother can impart an adequate amount of that security in her manner of handling the infant. Breast feeding is a maturation point in the sequence of maternal development, which is important physiologically and psychologically to mothers. Concrete proof of the psychologic value of breast feeding as a technic is badly needed.

Contraindications include pathologic conditions in the breast or nipple and some disease processes in the mother. An insufficient supply of breast milk requires complemental feeding if persistent efforts do not increase the supply. Minor objections to breast feeding arising from faulty antepartum attitudes, mistaken ideas and failure to appreciate the emotional value of nursing in child care can best be met in the prenatal clinic. They cannot be handled as adequately after the baby is born.

FROM THE AUTHORS' SUMMARY.

THE QUALITY OF THE DIET AND THE CONSUMPTION OF SUCROSE SOLUTIONS. C. M. MCCAY and EVA M. EATON, J. Nutrition **34**:351 (Oct.) 1947.

McCay and Eaton observed that rats fed an adequate stock diet drink about 12 cc. of water, or 24 cc. of 10 per cent sucrose solution, per day per 100 Gm. of

live weight. The water consumption of growing rats in relation to body weight declines progressively as the rats mature, while the amount of sugar solution drunk is relatively constant. Rats fed low calcium diets refuse to consume cola beverage or sucrose solution except in amounts to provide water; the amount of sucrose solution drunk is lower than the normal water consumption. In the case of growing rats a high level of sucrose solution was drunk only when the diet was supplemented with protein, vitamin A and calcium.

FREDEEN, Kansas City, Mo.

BALANCE AND ELECTROCARDIOGRAPH STUDIES IN A CHILD WITH POTASSIUM DEFICIENCY. WILLIAM WALLACE and FREDERIC C. MOLL, Pediatrics **4**:287 (Sept.) 1949.

In a 4 year old child with extrophy of the bladder in whom a ureterosigmoid transplantation had been carried out severe vomiting, diarrhea and fever developed. He was treated for dehydration with dextrose and isotonic sodium chloride solutions intravenously. On the third day of treatment, muscular and respiratory weakness appeared; the blood potassium was found to be 0.75 milliequivalent, and the electrocardiogram was abnormal. Chief electrocardiographic findings were prolonged Q-T interval, depressed S-T segments and low diphasic T waves. These findings are diagnostic of potassium deficiency. Response to intravenous administration of potassium was dramatic. Muscular weakness disappeared within an hour, as did the electrocardiographic changes, although the serum potassium level did not return to normal for four days. Measurement of the potassium balance during the four-day period in which the recovery was studied showed that potassium was retained to the extent of 16 per cent of the expected body content of this ion. Data indicate that recovery of impaired muscle function had occurred long before any significant portion of this retention had been accomplished.

FROM THE AUTHORS' SUMMARY.

THE DYNAMICS OF CIRCULATION IN INFANTILE MALNUTRITION. KERPEL E. ERONIUS, Pediatrics **4**:301 (Sept.) 1949.

Signs of disturbed circulation appear in marasmic infants usually with a degree of wasting of more than 30 per cent of the ideal weight. The condition is characterized by decreased blood pressure, cardiac output and stroke volume, by longer circulation time and by increased capillary permeability for fluids and protein. The blood volume appears to be somewhat increased. A decrease in the physical work of the heart was found to be parallel to the wasting of the heart. Inequality of wasting of different organs results in a large brain, kidneys and body surface per unit of body weight, in contrast to an atrophic heart and atrophic muscle system. The possible consequence of changed body proportions to circulation is discussed. The origin of circulatory disturbance in malnutrition is shown to be different from that observed in infantile toxicosis. The state of circulation in infantile marasmus seems to be one of the limiting factors in the rebuilding of the body and one of the causes of the high fatality rate following intercurrent banal infections.

FROM THE AUTHOR'S SUMMARY.

"EFFECT OF INCUBATION ON THE CHOLESTEROL PARTITION IN HUMAN SERUM." KENNETH B. TURNER and VIRGINIA PRATT, Proc. Soc. Exper. Biol. & Med. **71**:633 (Aug.) 1949.

Incubation of normal human serum and that from patients without hepatic disease resulted in a drop in free cholesterol of 30 per cent, with no change in

the total cholesterol. A smaller decrease in free cholesterol was found in patients with parenchymatous liver disease and occasionally in those with extrahepatic obstructive jaundice. The decrease in free cholesterol did not parallel changes in serum bilirubin, alkaline phosphatase, serum albumin or the result of the cephalin flocculation test.

HANSEN, Galveston, Texas.

A HOMOGENEOUS EMULSION OF FAT, PROTEIN, AND GLUCOSE FOR INTRAVENOUS ADMINISTRATION. G. P. SHAFIROFF and CECIL FRANK, Science **106**:474 (Nov. 14), 1947.

The authors present a preliminary report of what appears to be a well tolerated mixture of glucose, protein and fat for intravenous use. Prepared by mechanically homogenizing refined coconut oil, Knox® infusion gelatin, protein hydrolysate and glucose, the mixture is apparently stable on refrigeration and contains approximately 5 per cent each of protein, fat and carbohydrate to yield 750 calories per liter. A trial in 12 human patients produced no untoward effects, nor were pathologic changes noted in the tissues of 5 experimental animals (dogs).

FORBES, St. Louis.

USE OF CASEIN HYDROLYSATE AS A STANDARD IN THE STUDY OF THE SPECIFIC DYNAMIC ACTION OF FOODS. L. SALMI, Clin. pediat. **30**:628 (Oct.) 1948.

The respiratory metabolism was determined before and one-half, two and three hours after the intravenous injection of 25 cc. of a 5 per cent solution of casein hydrolysate in each of 12 fasting children. The metabolism increased 12 per cent over the basal rate in the first thirty minutes, 31 per cent after one hour and 14 per cent after two hours; it had returned to normal after three hours.

These observations indicate the specific dynamic action of the amino acids of protein, without allowance having to be made for the complicating factors of the energy expended in digestion and absorption.

HIGGINS, Boston.

CALCIUM IONS IN GUANIDINE INTOXICATION. ANNA SARPERI, Policlinico inf. **16**:140 (March) 1948.

The author reports a method of measuring the amount of calcium iron in the blood and describes several of her experiments on the quantity of this element in the blood of mice intoxicated with guanidine. She reaches the following conclusions: The total calcium in the blood of these mice decreased from an average 12.24 mg. to an average 10.3 mg. per hundred cubic centimeters. There was a slight increase in protein, which was often absolute and always relative to the quantity of total calcium in the blood. The decrease in the calcium ions was always constant, although not very great.

FROM THE AUTHOR'S SUMMARY.

METABOLISM OF KETONE BODIES IN CHILDHOOD. P. TOLENTINO, G. COTELLESSA and G. CAFFARENA, Policlinico inf. **16**:323 (July) 1948.

In order to study the pathogenesis of several syndromes which are characteristic of childhood and which are probably connected with alterations in the metabolism of lipids (cyclic vomiting with acetonemia, symptomatic ketosis, slight hepatic insufficiency), the authors proposed a systematic investigation of the variations

in the metabolism of ketone bodies by means of the intravenous content of acetone. They report in this paper on the results they obtained in 10 well children receiving a normal diet. After the injection of 0.05 cc. of acetone per kilogram of body weight, an increase of ketonemia appeared which involved both acetone and diacetic acid, while the increase in beta-oxybutyric acid was less constant (sometimes at the beginning a diminution of this fraction could be observed). The increase in ketonemia was nevertheless a modest one, continuing sometimes up to twelve hours. The mean values are reported, with their respective standard deviation, for the initial ketonemia, for the maximum increase reached and for the difference between the basal value and the twelfth hour value. The authors will use this data for a comparison in future researches of children having pathologic manifestations with these same normal children under different dietetic conditions.

FROM THE AUTHORS' SUMMARY.

Vitamins; Avitaminoses

CREATINE METABOLISM IN THE INFANT TREATED WITH LARGE DOSES OF VITAMIN D_2. EGIDIO COSSANDI, Policlinico inf. **16**:227 (March) 1948.

The author studied creatine metabolism in healthy children of different ages given one large dose of vitamin D_2. In this series all the subjects treated with vitamin D_2 showed a constant and clearcut increase in creatinemia of a transitory nature. Comparative investigations on percentages of phosphatemia have shown no evident relation to the creatinemia.

FROM THE AUTHOR'S SUMMARY.

EFFECT OF ASCORBIC ACID ON THE ABSORPTION OF IRON. G. BUGYI, Paediat. Danub. **6**:97 (Aug.) 1949.

To gain information on the possible role of vitamin C in the absorption of iron, the changes occurring in the blood level of nonhemoglobin iron were examined before and after oral administration of ascorbic acid. Ingestion of that substance was followed by a significant rise in the blood iron level. The effect is due neither to liberation of stored iron nor to some influence on gastric secretion, but absorption of iron from the intestines is enhanced by the presence of vitamin C. The concentration of iron in the blood depends on the blood level of ascorbic acid according to the equation: blood iron in micrograms per hundred cubic centimeters $= 50 + 5.1$ mg. per milliliter of ascorbic acid.

FROM THE AUTHOR'S SUMMARY..

Prematurity and Congenital Deformities

THE OPERATIVE TREATMENT OF PECTUS EXCAVATUM. MARK M. RAVITCH, Ann. Surg. **129**:429 (April) 1949.

Pectus excavatum (funnel breast) is a deformity of the thorax marked by a sharp posterior curve of the body of the sternum, deepest just before its junction with the xiphoid. The deformity is present at birth and usually is progressive. It may be satisfactorily corrected by operation. The younger the patient, the greater the likelihood of attaining a completely normal thoracic contour. Operation is indicated for removal of a cosmetic defect, for correction of a skeletal deformity and for alleviation of cardiac or pulmonary symptoms. The author describes his technic and reports on operation in 8 children. The article is well illustrated.

BANTIN, Omaha.

HEREDITARY PHALANGEAL AGENESIS SHOWING DOMINANT MENDELIAN CHARACTERISTICS. NESTA H. WELLS and MARGARET PLATT, Arch. Dis. Childhood **22**:251 (Dec.) 1947.

A description is given of an inherited deformity of the extremities, showing a combination of ectrodactyly and polydactyly, passing through six generations as a heterozygous dominant with some male preponderance. The gene appears to be linked with one producing musical capability.

KELLY, Milwaukee.

CONGENITAL WEBBING OF THE LOWER LIMBS. EMLYN LEWIS, Proc. Roy Soc. Med. **41**:864 (Dec.) 1948.

Congenital webbing of the lower limbs was reported in a girl 7 years of age. The patient was referred to the hospital because of her inability to walk without crutches and the contractures of her lower limbs. She also had a bilateral incomplete harelip and the posterior two thirds of the palate was cleft. The description of the webbing and details of the operation that was performed are given in the report. The patient is now able to walk unaided.

WILLIAMSON, New Orleans.

PEPSIN AND PANCREATIC PROTEINASE IN PREMATURE INFANTS COMPARED WITH THAT IN FULL TERM INFANTS. BIRGITTA WERNER, Ann. pædiat. **170**:8 (Jan.) 1948.

The secretion picture in the gastric mucous membrane and the pancreas were examined with regard to pepsinogen and pancreatic proteinase, respectively, in a series of 42 premature and 19 full term infants. The histologic changes were controlled in a number of the subjects by chemical determination of the enzyme content. The material shows a great difference between premature infants weighing under approximately 2,300 Gm. and full term infants with regard to the stage of development of the proteolytic enzyme system.

FROM THE AUTHOR'S SUMMARY.

STUDIES ON HUMAN ABORTION OVULA WITH PARTICULAR CONSIDERATION OF THE EARLY MALFORMATIONS AND THEIR CAUSES. O. KAESER, Schweiz. med. Wchnschr. **79**:1050 (Nov. 5) 1949.

Exogenous factors in the production of ova expulsed mainly during the second and third month of pregnancy are discussed; then the endogenous factors residing in the gametes or zygotes are discussed. The role of defective sperm cells in the production of abortion is also discussed.

AMBERG, Rochester, Minn.

COMMON TRAITS OF BODY COMPOSITION OF PREMATURE AND ATROPHIC INFANTS. S. KOVACH and B. VARBIRO, Paediat. Danub. **6**:91 (Aug.) 1949.

The volume of extracellular fluid, in several infants born in the seventh fetal month, was determined by the thiocyanate method on the first day of their life. It was established that at that age extracellular water forms half of the body weight. The striking similarity between the body composition of premature and of atrophic infants is demonstrated. The high morbidity rate common in both conditions might be in connection with the special body composition.

FROM THE AUTHOR'S SUMMARY.

FETAL MALFORMATIONS WITH ABNORMAL CALCIFICATIONS AS A RESULT OF INTRAUTERINE INFECTIONS. CONRAD GASSER and ERICH SCHWARZ, Helvet. paediat. acta **2**:351 (Aug.) 1947.

Gasser and Schwarz record the clinical, pathologic and anatomic study of peculiar deformities of an 8 month old baby whose mother had had an eruptive disease in the third month of pregnancy. The baby, who was underweight at birth, showed at first signs of asphyxia, had difficulty in assimilating food and remained backward in physical and mental development. The syndrome consisted of peculiar calcifications in the brain, eye and liver, partly with chronic inflammatory indications; moreover, there was an enormous hydrocephalus with fluid changes. The ocular changes, with microphthalmia and cataract, point to an early injury to the fetus. Attention is drawn to the connection between congenital toxoplasmosis and the syndrome of the deformities following German measles during pregnancy. A brief outline of the differential diagnosis of the diseases with calcifications of the brain is given.

FROM THE AUTHORS' SUMMARY.

HEREDITARY KOILONYCHIA COMBINED WITH CONTRACTURES OF THE LITTLE FINGERS AND TOES. L. S. WILDERVANCK, Nederl. tijdschr. v. geneesk. **92**:334 (Jan. 31) 1948.

Hereditary koilonychia without changes in the hemoglobin content and the number of erythrocytes is reported by many investigators.

Some members of the affected families showed koilonychia only; others suffered from contractures, and several persons had flat and very brittle nails only, a condition considered an abortive form of the koilonychia.

The anomaly is regularly dominant. It is thought to be caused by mutation of one gene, influencing the ectodermal properties and affecting in some cases the adjoining gene, thereby influencing the mesodermal structures.

The first family described by Wildervanck consisted of 72 members, of which 25 showed the anomaly. Only 5 of them had the combination of koilonychia and contracture of the little fingers. One member had a contracture of his thumb, and 2 members had contractures of the little toes. Eleven of the 17 members of the second family showed the anomaly. One member had other congenital defects of his hands and feet also and had koilonychia of the toes.

All the persons mentioned had normal hemoglobin values and were in good health.

VAN CREVELD, Amsterdam, Netherlands.

Newborn

CICATRIZING ENTEROCOLITIS IN A NEWBORN INFANT. C. EVERETT KOOP, JOSEPHINE G. PERLINGIERO and WILLIAM WEISS, Am. J. M. Sc. **214**:27 (July) 1947.

A unique report of chronic enterocolitis involving the entire small and large bowel in a newborn infant is given. It seems likely that this lesion had its origin in prenatal life.

HENSKE, Omaha.

URINALYSIS IN DEHYDRATION FEVER. JOHN THOMSON, Arch. Dis. Childhood **22**:226 (Dec.) 1947.

In 2 cases of dehydration fever in the newborn, the daily output of urine, with its specific gravity and urea and chloride concentration, was recorded. These observations were related to the time of onset and subsidence of the pyrexia. The

figures for the urinalyses were compared with those for normal average apyrexial newborn babies. From the observations made it appears that the kidney of the newborn infant is capable of concentrating the urine to a much greater extent than is generally recognized.

KELLY, Milwaukee.

HERNIA INTO THE UMBILICAL CORD AND OMPHALOCELE (AMNIOCELE) IN THE NEWBORN. CLIFFORD D. BENSON, GROVER C. PENBERTHY and EDWARD J. HILL, Arch. Surg. **58**:833 (June) 1949.

The term omphalocele, or amniocele, should be restricted to those congenital defects in which there is herniation of the abdominal viscera into a sac covered by peritoneum and amniotic membrane through the umbilical and supraumbilical portion of the abdominal wall. In contrast, a hernia into the umbilical cord has a defect limited to the umbilical opening. The incidence of hernia into the umbilical cord and omphalocele has been estimated to be about 1 in 6,000 births.

The time of origin of omphalocele is in the third week of embryonic life, whereas hernia into the umbilical cord occurs in the eighth to the tenth week. Early operation and the extent of the surgical procedure will be dictated by (*a*) the condition of the patient, (*b*) the presence of viscera in the sac, (*c*) coexistent anomalies and (*d*) the size of the defect.

KAISER, Rochester, N. Y.

PROPHYLAXIS AGAINST OPHTHALMIA NEONATORUM: CLINICAL COMPARISON OF PENICILLIN AND SILVER NITRATE, A PRELIMINARY REPORT. H. CHARLES FRANKLIN, J. A. M. A. **134**:1230 (Aug. 9) 1947.

This is a report on a study of 1,710 infants, 961 of whom received penicillin prophylactically against ophthalmia neonatorum and 749 of whom received silver nitrate. The silver nitrate was used as a 1 per cent solution prepared fresh daily. The penicillin solution used contained 2,500 units per cubic centimeter. The solution was kept refrigerated, and fresh solution was made at least weekly. Silver nitrate instillations were done only in the delivery room. Penicillin instillations were done in the delivery room and repeated daily for the first three days.

Of the infants receiving penicillin, 2.1 per cent exhibited pus in one or both eyes. About half of these babies showed the pus during the first and second days of life. Six per cent of the infants receiving silver nitrate showed pus in one or both eyes almost entirely on the first and second days of life. Swelling of the eyelids, redness of the conjunctiva and watery discharge were less frequent following penicillin prophylaxis. Gonococcic infection developed in 1 premature baby who had received silver nitrate.

Of those infants who could be followed after their discharge from the hospital, 3.1 per cent of those receiving penicillin showed pus in the eye at the fourteenth to seventeenth days. Four of these were hospitalized. Of the babies receiving silver nitrate 1.5 per cent showed pus at the fourteenth to seventeenth days. Two of these were hospitalized. None in either group had gonococcic infection.

BAIRD, Wauwatosa, Wis.

CONGENITAL MORPHINISM: A RARE CAUSE OF CONVULSIONS IN THE NEWBORN. MEYER A. PERLSTEIN, J. A. M. A. **135**:633 (Nov. 8) 1947.

The literature on congenital morphinism is reviewed. The case reported is that of a baby born to a mother who took during her pregnancy, including the day of delivery, 10 grains (0.65 Gm.) of morphine intravenously daily. Symptoms of

irritability, restlessness, vomiting and passing of liquid stools developed on the third day of life. Generalized tremors and occasional convulsions occurred. The administration of phenobarbital, ⅛ grain (8 mg.) every four hours, allayed all symptoms. Occasional tremors continued until the age of 1 month. Use of phenobarbital was tapered off after eight weeks. Nystagmus, head nodding and spasmus nutans were noted. These gradually abated by the time the child was 1 year old. General development was normal.

BAIRD, Wauwatosa, Wis.

THE PATHOGENESIS OF THE "VERNIX MEMBRANE": RELATION TO ASPIRATION PNEUMONIA IN STILLBORN AND NEWBORN INFANTS. HERBERT C. MILLER and TOM R. HAMILTON, Pediatrics **3**:735 (June) 1949.

The clinical records of 79 stillborn and liveborn infants were correlated with the postmortem observations on their lungs. Evidence of aspiration was noted chiefly in the lungs of full term stillborn infants in the form of large numbers of blue-staining cornified epithelial cells, together with large amounts of fat in the terminal air spaces. Hyaline-like membranes were seen in the terminal air spaces in greatest numbers in the lungs of liveborn premature infants who had no history of any maternal complication of pregnancy or labor.

It is suggested that the hyaline-like membranes may not be composed of aspirated vernix and amniotic sac contents but probably represent a reaction to an injury to the epithelium of the air spaces, especially the bronchioles and alveolar ducts.

The nature of the etiologic agent remains doubtful, but the similarity of these membranes to those observed in older persons who died of pandemic influenza and with rheumatic pneumonitis suggests that intrauterine inflammatory reaction may be a factor. The relationship to congenital alveolar dysplasia is discussed. It is suggested that the hyaline-like material is phagocytosed by polymorphonuclear leukocytes and mononuclear cells. The presence of these phagocytes in the alveoli and bronchi in association with hyaline-like material is one of the chief forms of pneumonia in the newborn infant.

FROM THE AUTHORS' SUMMARY.

RUPTURE OF ANEURYSM OF THE CIRCLE OF WILLIS IN THE NEWBORN. ALVAH L. NEWCOMB and GEORGE F. MUNNS, Pediatrics **3**:769 (June) 1949.

An instance of rupture of aneurysm of the circle of Willis occurring in a newborn infant is presented. Such spontaneous vascular accidents are extremely rare; no previous report of such a phenomenon has been found. This case occurred in a male of twins, both of whom died within thirty-one hours after birth, each twin presenting identical symptoms. Unfortunately, an autopsy on the head was not performed on the female twin. The one performed on the male infant revealed a ruptured aneurysm occurring at the junction of the posterior cerebral artery and posterior communicating branch on the right. This case lends support to the opinion that most "berry" intracranial aneurysms are congenital in origin.

FROM THE AUTHORS' SUMMARY.

CONGENITAL HEMOLYTIC DISEASE RESULTING FROM A-O ISOIMMUNIZATION. NATHAN MITCHELL, ARMAND H. MOSS, BERNARD REDNER, HAROLD LEVY and I. J. GREENBLATT, Pediatrics **3**:813 (June) 1949.

Three instances of fatal hemolytic disease of the newborn were observed in group A infants born of Rh-positive mothers belonging to group O. Greatly

elevated anti-A agglutinins were demonstrated in the mother's serum following delivery of the child (1:10,120 in case 1, 1:5,000 in case 2 and 1:6,000 in case 3). All these titers fell within three weeks. All infants were Rh positive and no Rh or Hr antibodies were found in the mother's serum. Jaundice became apparent within twenty-four hours of birth in all infants. There was a moderate anemia, and varying numbers of nucleated red cells were observed in the peripheral blood. One infant died on the third day of life, the second on the fifth and the third on the sixth. Typical changes of hemolytic disease of the newborn were present at autopsy, and extensive kernicterus of the basal ganglions, hippocampal nuclei, periventricular pontile nuclei, cerebellar dentate nuclei and medullary olives was noted. The observation of free circulating antibodies in the infant's blood obtained post mortem is of particular interest. These anti-A agglutinins were active only in albumin-plasma dilutions. The retention of the agglutinating property of this antibody in both infant and mother even after the addition of the A and B blood group specific (Witebsky) substances indicates that it is probably an immune antibody. It is believed that A-O isoimmunization is proved in these 3 cases.

From the Authors' Summary.

Bedside Cabinet for the Newborn Infant Designed for Rooming-In Facilities. Preston A. McLendon and John Parks, Pediatrics **4**:106 (July) 1949.

In adopting the principle of rooming-in and selective feeding procedures, it is necessary to provide an infant carriage that will render convenient and practical methods of infant handling. The bassinet in use in the maternity service at the George Washington University Hospital, Washington, D. C., was designed to fulfil the following demands: (1) simplicity; (2) ease of cleaning; (3) mobility; (4) compartments for storing nursery equipment sufficient for the complete care of the infant; (5) foolproof attachment to the mother's bed in adjustable positions; (6) movable bassinet on top of the cabinet for convenient and easy lifting out and replacement of the infant; (7) clear plastic bassinet for observation of the infant by nurse and mother.

From the Authors' Summary.

Study of Pulmonary Hyaline-Like Material in 4117 Consecutive Births: Incidence, Pathogenesis and Diagnosis. Herbert C. Miller and M. Harry Jennison, Pediatrics **5**:7 (Jan.) 1950.

A study has been made of 4,117 consecutive births, including 66 stillborn infants and 85 neonatal deaths. Autopsies were done on 22 of the stillborn infants and on 71 infants who died during the neonatal period. From the autopsy study of neonatal deaths it was found that at least 15 per cent of all liveborn premature infants weighing between 1,000 and 2,000 Gm. at birth had hyaline-like material in their lungs. The incidence of the pulmonary lesion was noted to diminish progressively as the weight at birth of the infants increased, so that it was practically nonexistent in infants weighing over 3,000 Gm. at birth.

It was observed that 90 per cent of all infants weighing over 1,000 Gm. at birth who died in the first forty-eight hours of life had hyaline-like material in their lungs at autopsy provided their mothers' pregnancies and labors had been free of serious complications and provided the infants themselves had no other clinically recognized disease or defect of a serious nature. No relation was seen between the presence of the pulmonary lesion and the race, sex, order of birth of the infant or the age of the mother and length or type of labor. The lesion was not produced by the aspiration of food.

The symptomatology in the infants who died with hyaline-like material in the lungs was characterized by severe respiratory difficulty, including retraction of the lower wall of the chest with inspiration. The symptoms were not pathognomonic, but few premature infants with similar symptoms survived.

The pathogenesis of this pulmonary lesion remains unknown. The theory advanced, based on the facts brought out in this study, is that the hyaline-like material in the lung is the result of an etiologic agent that not only injures the lung of the fetus but also causes the premature birth of the infant so injured.

FROM THE AUTHORS' SUMMARY.

PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM. ARNOLD SORSBY, Brit. M. J. **2**:322 (Aug. 30) 1947.

In an exhaustive study, Sorsby continues his investigations on penicillin therapy of ophthalmia neonatorum. The results of the study are carefully tabulated and discussed under the headings of the local treatment with penicillin in aqueous solution at five and at one minute intervals, the type of organism involved, the use of penicillin in vehicles other than water and the systemic injection of penicillin. The author discusses the course of the disease with the different modes of application, relapses and unsatisfactory response, response in relation to the causal organism, the choice of method in intensive local therapy and in massive systemic injection and a comparison of penicillin therapy with general sulfonamide treatment.

In the summary it is stated that in the present series of 232 patients 224 were treated by various methods of application of the drug: 101, by instillation of aqueous drops in a concentration of 2,500 units per cubic centimeter at five or at one minute intervals; 33, with more concentrated drops, 10,000 units per cubic centimeter, and 51, with oily or solid vehicles containing penicillin, the last with unsatisfactory results. In a final series of 39 patients massive systemic injections were given, followed by instillation of a strong solution of penicillin on completion of the course.

"A total failure to respond to penicillin treatment has not been observed, and in no case has penicillin treatment failed to influence the condition sufficiently to remove all anxiety within a matter of hours, or less. The optimum mode of use of penicillin is still to be determined, though even now the results obtainable are as great an advance on those of the sulphonamides as these in turn were over the classical methods of treatment."

KNAPP [ARCH. OPHTH.].

PENICILLIN AND OTITIS OF THE NEWBORN. BOURSIER, RIVIÈRE, L. CHASTRUSSE and J. MOLIA, Pédiatrie **36**:207 (May-June) 1947.

Penicillin treatment has improved the prognosis of otitis and otoantritis in the newborn. The authors stress the need for early intervention before antritis has developed. Paracentesis is of first importance and should be performed as soon as the diagnosis of otitis is established or even suspected. Local penicillin therapy is instituted, and intramuscular injections of 120,000 units a day are given. If after forty-eight hours improvement is not evident by an increase in weight of the infant, antrotomy with drainage by a penicillin-saturated gauze is indicated. Hydration, blood transfusion, temperature regulation and isolation should be observed as general measures at all times.

GLASER, Chicago.

PRENATAL TREATMENT OF HEMOLYTIC DISEASE OF THE NEWBORN. ORAZIO MALAGUZZI VALERI, Arch. ital. pediat. puericolt. **12**:209, 1948.

A case is recorded of an Rh-negative woman who was married to an Rh-positive homozygous man and whose 3 children, born after her first three pregnancies, died from hemolytic disease of the newborn. During her fourth pregnancy, she was treated in the last seven months by Wiener's prophylactic method, i. e., she received injections of antityphus vaccine until antityphus agglutinins of 1:6,400 were formed. Neither during the pregnancy nor after the confinement was there any evidence of anti-Rh agglutinins. Although the fetus was Rh-positive (Rh_0), it was apparently healthy at birth, without any erythroblastemia or other evident symptoms of disease. With a wetnurse, the child grew and gained normally. The serologic findings tend to exclude the possibility that the mother was isoimmunized toward an Rh subgroup not present in the child. It is also extremely improbable that she was immunized toward irregular groups. The possibility is pointed out that the formation of Rh antibodies was inhibited by the intense antityphus immunizing reaction caused by the early and prolonged vaccination treatment.

FROM THE AUTHOR'S SUMMARY.

DEATH FOLLOWING TRANSFUSION OF RH-INCOMPATIBLE BLOOD. KARL PRETL, Wien. klin. Wchnschr. **62**:14 (Jan. 6) 1950.

A woman 27 years of age, with a history of a miscarriage and two stillbirths, had severe menstrual bleeding followed by intense epistaxis. She received several transfusions from 3 different donors, the last of 10 cc. of fresh blood. Two hours later the patient died. The blood of one donor was Rh positive, while that of the patient taken post mortem was Rh negative with an anti-D agglutinin titer of 1:500. Stress is laid on the renal changes. Even in cases in which so-called weak antigens are present an influence of an existing disease may be of importance as a secondary factor.

AMBERG, Rochester, Minn.

Acute Contagious Diseases

PSYCHOLOGIC ASPECTS OF POLIOMYELITIS. MORTON A. SEIDENFELD, Pediatrics **4**:309 (Sept.) 1949.

While many more contributions may be made by the physician in caring for the child with poliomyelitis, there are at least five principal areas in which he plays a major psychologic role in addition to his ordinary responsibilities in regard to medical care of the patient: (*a*) in dealing with the relief of the patient's psychologic reactions to the acute phase of the disease; (*b*) in reducing psychologic trauma attendant on the removal of the patient from his normal environment and placing him in the treatment environment of the hospital or nursing institution; (*c*) by explaining and correcting misconceptions that the patient may have about his illness and its ultimate effects; (*d*) by aiding the parents to avoid erroneous concepts, feelings of personal guilt and improper attitudes toward their child and the family as a whole during the child's illness, and (*e*) by correcting community misconceptions regarding the needs of the child with poliomyelitis and by fostering adequate community cooperation in helping disabled children make the best possible socioeconomic and psychologic adjustment to life.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF WHOOPING COUGH WITH STREPTOMYCIN. RUBÉN GAMBOA ECHANDIA, Pediat. Américas **7**:142 (March) 1949.

Fifteen patients, from 3 months to 7 years of age, were treated with intramuscular injections of streptomycin, 1 Gm. daily in eight doses, for a total of five days. Three patients with bronchopneumonia received the antibiotic for eight days. The cough decreased in the first three days and all patients were cured between the fifth and the tenth day after the initiation of therapy.

DE LA TORRE, México, D. F., Mexico.

CONTRIBUTION TO EPIDEMIOLOGY OF POLIOMYELITIS. ERNEST SAUER, Med. Klin. **44**:540 (April 29) 1949.

In a region with 98,000 inhabitants, 122 cases of poliomyelitis were seen from the beginning of July to the middle of September 1948. The importance of transmission by flies is strongly emphasized, demanding thorough disinfection of the dejecta, as well as rigorous antifly measures.

AMBERG, Rochester, Minn.

SHOULD CHILDREN BE IMMUNIZED AGAINST SCARLET FEVER? FRITZ HUBER, Med. Klin. **44**:546 (April 29) 1949.

In 13 of 38 children with scarlet fever the disease was mild. Six of these had been immunized sufficiently. In the remaining 25 patients the disease had a typical course and only 1 of these was sufficiently immunized. But complications occurred in 2 of the 6 sufficiently immunized children and in 4 of the 24 who were not immunized or who were insufficiently immunized. At present, immunization is not regarded as absolutely necessary.

AMBERG, Rochester, Minn.

CHECK OF THE INTRAVENOUS TOXOID TREATMENT OF DIPHTHERIA ACCORDING TO CREMER. FRITZ LUCKE, Med. Klin. **45**:47 (Jan. 13) 1950.

Patients with diphtheria were treated with antiserum and with intravenous injections of "formol toxoid" (Behring). All the patients were older than 14 years. The intravenous "formol toxoid" treatment did not offer any advantage and was discontinued.

AMBERG, Rochester, Minn.

INTRASPINAL TREATMENT OF POSTDIPHTHERITIC PARALYSIS WITH TOXOID. SUSANNE PALM, Med. Klin. **45**:84 (Jan. 20) 1950.

Five cases of severe postdiphtheritic paralysis are reported in which the condition did not respond to usual remedies, including intravenous administration of toxoid. "Formol toxoid" (Behring) was then given intraspinally in a dose of 0.5 ml. The result was extraordinarily good. Only 1 of the patients was a child, a 3½ year old girl.

AMBERG, Rochester, Minn.

THE INTRAVENOUS TOXOID TREATMENT OF DIPHTHERIA. J. CREMER OFFENBACH, Med. Klin. **45**:144 (Feb. 3) 1950.

In recalculating the results of Wuensche and Muenkel, the author found the combination of toxoid and antiserum by intravenous injection about three times as effective as treatment with antiserum alone. The combined treatment is outlined.

AMBERG, Rochester, Minn.

POLIOMYELITIS-LIKE CEREBROSPINAL FLUID IN CATTLE ON FARMS WITH CASES OF HUMAN POLIOMYELITIS. E. FRAUCHIGER and G. SCHMID, Schweiz. med. Wchnschr. **79**:316 (April 9) 1949.

Spinal punctures were done in animals, mostly cows, in different locations. Only 2 cows of different farms where several inhabitants had paralysis had pathologic cerebrospinal fluids. In one farm a cow was ill with fever and muscular weakness, with consequent muscular atrophy. About the same time the father and son were taken ill with fever, headache and meningismus. A daughter was hospitalized for poliomyelitis. Four months later the cerebrospinal fluid of this cow was normal, but that of her neighboring stablemate deviated from the norm.

On the other farm 3 members of the family were taken ill with symptoms suggestive of poliomyelitis. In the adults paralysis developed. About one month later a cow became ill with a nervous disorder and recovered. In her spinal fluid taken two months later, some increase of preponderantly large epithelial cells was noted. A neighbor in the stable presented increased spinal fluid pressure and other abnormalities. Extended examination of cerebrospinal fluids of domestic animals should be conducted in times of epidemics.

AMBERG, Rochester, Minn.

WHEN SHOULD DIPHTHERIA ANTISERUM BE ADMINISTERED? F. HAUSER, Schweiz. med. Wchnschr. **79**:426 (May 14) 1949.

On the basis of observations on 481 children with diphtheria seen in the children's hospital in Basel, Switzerland, the author is of the opinion that in suspected cases of the disease antidiphtheritic serum should be injected immediately without waiting for the demonstration of bacilli. It is of special interest that 7 cases occurred in newborn children, 4 of these in the course of two weeks. This happened in the gynecologic clinic where the newborn infants were kept during the day with the mothers, before visiting by children was prohibited.

AMBERG, Rochester, Minn.

MEASLES ENCEPHALITIS. EMMA VESTERGAARD, Nord. med. (Hospitalstid.) **33**:296 (Jan. 31) 1947.

Encephalitis is reported in a girl 6 years of age, who one week after the eruption of measles exanthem fell ill with fever, drowsiness and convulsions. She was stuporous and adynamic for one week, and then showed psychomotor disturbances for three weeks. At her discharge from the hospital four months later she displayed slight paresis of the lower extremities and some impairment of memory. Nine months afterward she appeared healthy.

WALLGREN, Stockholm, Sweden.

POLIOMYELITIS IN INFANCY. NIELS B. KRARUP and P. PLUM, Nord. med. (Hospitalstid.) **33**:412 (Feb. 14) 1947.

Eighteen cases of poliomyelitis are reported in infants, aged 2 weeks to 10 months, of whom 4 were aparalytic. In 6 of the paralytic patients only the paralytic symptoms were first noted. In 4 patients fever occurred before paralysis. In 3 patients catarrhal symptoms and in 1 diarrhea were the first signs. In the aparalytic group fever occurred in 3 patients before stiffness of the neck was noted and in 1 patient there was diarrhea. In 4 of the paralytic patients no stiffness of the neck was observed. The paresis was generally localized in the

extremities, occasionally in the cranial nerves. The spinal fluid rarely was found to be normal. Two of the infants died and the postmortem examination displayed typical histologic changes. The authors discuss the differential diagnosis and stress the paramount importance of lumbar puncture. Of the 18 children 8 were admitted to the hospital with the diagnosis of poliomyelitis, 4 with meningitis, 2 with paresis, 1 with cerebral hemorrhage and 1 with muscular atrophy. In 2 patients no tentative diagnosis was made at admission. Two patients were newborn breast-fed infants with healthy mothers. In 1 child, aged 7 months, the disease manifested itself during hospital treatment for another illness. The source of infection was unknown. Treatment consisted of warm baths twice daily after the acute stage had passed. After paralysis was present four weeks, orthopedic treatment was instituted.

WALLGREN, Stockholm, Sweden.

PATHOGENESIS AND PROPHYLAXIS OF POLIOMYELITIS. SVEN GARD, Nord. med. (Hygiea) **34**:1399 (June 20) 1947.

Present evidence tends to show that the virus of poliomyelitis is strictly neurotropic and that the process of infection is confined entirely to the interior of nerve cells. Thus, the virus seems to enter the central nervous system through peripheral nerves and to spread within the central nervous system along the neuronal pathways. There is, furthermore, no doubt that the virus originally enters the body through the alimentary tract. The mechanism by which the virus travels from the mucous membranes of the mouth, throat and intestinal canal to the peripheral nerves is, however, obscure. Absorption through the lymphatic tissue of the throat, as well as the intestinal mucous membrane, and deposition of the virus in the regional lymph nodes seem to occur regularly. On the basis of observations made in connection with two different spontaneous outbreaks of poliomyelitis in a mouse colony, the hypothesis is advanced that disorganization of the lymph node in the course of an intercurrent disease of nonpoliomyelitic origin favors the accidental contact of virus and naked nerve fibers in the node. Accordingly, the true portal of entry of the virus is situated in the lymph nodes. Thus,. the first phase of the dromedary type (Draper) of poliomyelitis represents the onset of a disease of nondescript origin acting as a provocative factor. Intracellular virus is protected against the action of antibodies. Provided the aforementioned hypothesis is valid, it is still possible, however, to attack and neutralize the virus on its way to and in the lymph nodes; immunization with inactivated virus might, therefore, provide a practicable means of prophylaxis.

FROM THE AUTHOR'S SUMMARY.

ACUTE POLIOMYELITIS IN PREGNANCY. REIDAR GRELLAND, Nord. med. (Norsk mag. f. lægevidensk.) **33**:620 (March 7) 1947.

The author reports on 10 cases of poliomyelitis in pregnant women. One had a missed abortion; in 1 delivery was by cesarean section. In another the pregnancy had not yet ended at the time of publication. In 4 cases the infants were healthy. Histologic examination of 2 of the stillborn infants revealed no poliomyelitic signs. There is no evidence of intrauterine infection with poliomyelitis virus when the mother has the disease during pregnancy.

WALLGREN, Stockholm, Sweden.

ACUTE POLIOMYELITIS IN MOTHER AND NEWBORN INFANT. ARNE G. FRÖVIG, Nord. med. (Norsk mag. f. lægevidensk.) **34**:1115 (May 9) 1947.

In a family of 11 members a 26 year old man fell ill with typical poliomyelitis in the first part of October 1945. On October 5 his 22 year old sister had paralysis

of the legs and died of respiratory failure a fortnight later. The day this sister died another sister, aged 20, was delivered of a healthy full term infant. The mother complained of some headache and tiredness in her legs a few days before delivery and had paralysis of the legs two days after delivery. On the fourth day the infant had a fever that lasted three days and displayed paresis of the arms, legs and head on the eighth day of life. Both mother and infant survived with residual paresis. This may be the youngest patient with poliomyelitis ever reported on. The possibility of intrauterine infection is discussed.

WALLGREN, Stockholm, Sweden.

TREATMENT OF SCARLET FEVER. ANCHERSEN, Nord. med. (Norsk mag. f. lægevidensk.) **35**:1509 (July 11) 1947.

The results in 100 patients with scarlet fever given penicillin treatment in 1946 are compared with those in 100 patients without penicillin treatment in 1945. Both groups in other respects were treated and cared for in the same way. In the former group there were complications in 29 per cent; 60 per cent were afebrile after three days and 90 per cent after five days. In the control group the figures were 54, 30 and 60 per cent, respectively. The author is of the opinion that the penicillin treatment should be continued for one week and that most patients with scarlet fever may be discharged from the hospital in the course of two weeks. He maintains that penicillin treatment offers medical and economic advantages.

WALLGREN, Stockholm, Sweden.

Acute Infectious Diseases

HISTOPLASMOSIS IN CALIFORNIA CHILDREN. HELEN B. PRYOR, J. Pediat. **34**:12 (Jan.) 1949.

The Mississippi River Basin is the geographic center of histoplasmosis in this country. Pryor gave skin tests to 85 California children suspected of the disease on the assumption that mild infections with this fungus may occur in other sections of the country. Five children with multiple pulmonary calcifications gave negative reactions to the tuberculin test and negative reactions to the test for histoplasmosis.

MACDONALD, Pittsburgh.

TYPHOID FEVER TREATED WITH CHLOROMYCETIN. RALPH STILLER, J. Pediat. **35**:85 (July) 1949.

A 6½ year old white girl with typhoid was given chloramphenicol chloromycetin.® She recovered promptly.

MACDONALD, Pittsburgh.

AN OBSERVATION OF ANTITOXIN TITERS AFTER BOOSTER DOSES OF TETANUS TOXOID. H. J. BANTON and PAULINE A. MILLER, New England J. Med. **240**:13 (Jan. 6) 1949.

Five-tenths cubic centimeter of tetanus toxoid was administered to 5 adults who had completed a basic immunizing course of tetanus toxoid from one year eight months to five years eight months prior to the booster dose. The residual antitoxin titer was computed and the rising titer checked from the fourth to the tenth days. The five day lag in rise which was noted suggests that the residual titer is of paramount importance in the prevention of overwhelming early clinical

disease, and the authors suggest that maintenance doses every three or four years should be insisted on in addition to a booster dose after injury.

WHEELOCK, Denver.

THE SPEED OF THE SECONDARY IMMUNE RESPONSE TO TETANUS TOXOID WITH A REVIEW OF THE WAR REPORTS AND OBSERVATIONS ON SIMULTANEOUS INJECTIONS OF TOXOID AND ANTITOXIN. JOHN J. MILLER JR., MARY LOUISE RYAN and R. R. BEARD, Pediatrics **3**:64 (Jan.) 1949.

A review of the 30 reported cases of tetanus occurring in actively immunized personnel of the British and American armies permits the following conclusions: The only type of tetanus that need be feared in recently immunized persons is that which may occur following extensive trauma or massive contamination. It is characterized by short incubation periods, sometimes less than one week, and a high fatality rate. Reinjection of toxoid on wounding in 2 such instances failed to prevent death. Speed of antitoxin response during the week subsequent to a reinjection of tetanus toxoid was observed in more than 150 actively immunized children. Striking individual differences were noted. Contributing factors were:

1. Type of toxoid employed in basic immunization; alum-precipitated or aluminum hydroxide-adsorbed toxoid induced a superior capacity for prompt reaction when compared with fluid toxoid.

2. Type of toxoid used for reinjection (for the secondary stimulus); fluid toxoid induced a more rapid rise in antitoxin than alum-precipitated toxoid.

3. Interval elapsing since the last previous injection of toxoid; when this was greater than four years, the speed of response was occasionally slowed.

Experimental evidence is advanced indicating that simultaneous injection of prophylactic antitoxin and tetanus toxoid in different extremities does not prevent a secondary immune response to toxoid. It is, therefore, suggested that maximal prophylactic effect against tetanus in severely wounded immunized persons (and/or when immunization occurred more than four years previously) may be obtained by simultaneous injection of toxoid and antitoxin in different extremities.

FROM THE AUTHORS' SUMMARY.

MODE OF ACTION OF STREPTOMYCIN ON H. INFLUENZAE TYPE B: III. NATURE OF STREPTOMYCIN ACTION ON SENSITIVE H. INFLUENZAE. HATTIE E. ALEXANDER and GRACE LEIDY, Pediatrics **3**:277 (March) 1949.

The data presented demonstrate that members of type B Hemophilus influenzae populations are not uniformly sensitive to streptomycin. Over 99 per cent are susceptible to 1.6 micrograms per cubic centimeter; the larger the population, the wider the variation in resistance of the small fraction surviving. The injurious action of streptomycin on type B H. influenzae is primarily bactericidal.

Streptomycin in concentrations between 10 and 100 micrograms per cubic centimeter exerts a rapid lethal action; the greater the concentration of the antibiotic, the greater the speed. Significant increases in the size of the population increase the time required for bactericidal action. The data presented suggest that when streptomycin is used in treatment of H. influenzae infections in man, its intramuscular administration over a period not longer than twenty-four hours will ordinarily suffice to obtain a maximal streptomycin effect; that in cases of meningitis the addition of a single intrathecal dose of streptomycin of 25 mg. will be adequate, and that use of sulfadiazine as an adjuvant is advisable to bring under control the eventual resistant mutants which may survive the bactericidal action of streptomycin.

FROM THE AUTHORS' SUMMARY.

STUDIES IN THE RELATION OF THE HEMOLYTIC STREPTOCOCCUS TO RHEUMATIC FEVER: VI. COMPARISON OF STREPTOCOCCAL ANTIHYALURONIDASE WITH ANTIBODIES TO OTHER STREPTOCOCCAL ANTIGENS IN THE SERUM OF PATIENTS WITH RHEUMATIC FEVER AND ACUTE STREPTOCOCCAL INFECTION: MUCIN CLOT PREVENTION TEST. T. N. HARRIS, SUSANNA HARRIS and RUTH L. NAGLE, Pediatrics **3**:482 (April) 1949.

Serums obtained from convalescents from streptococcic infections and from patients with acute rheumatic fever were tested for antibodies to four streptococcic antigens. These antigens are the hyaluronidase and hemolysin, derived from the supernate of streptococcic cultures, and two fractions, the cytoplasmic particles and the supernate proteins, prepared from the streptococcic cell. It was observed that the mean titers to all these antigens were elevated in both rheumatic and streptococcic infection. In the case of the antistreptolysin titer, as well as the titers to cytoplasmic particles and supernate protein, the mean titer was somewhat higher in rheumatic than in streptococcic infection. However, the mean antihyaluronidase titer obtained in the rheumatic group was considerably greater than that noted in the group of convalescents from streptococcic diseases. The possible significance of this observation from the point of view of causation and diagnosis in rheumatic fever is discussed.

FROM THE AUTHORS' SUMMARY.

AFTER-TREATMENT OF CHILDREN WITH ACUTE RHEUMATIC ARTHRITIS. J. D. VYMĚTAL, Pediat. listy **4**:73, 1949.

A review is given of the experience gained in a long term program of special treatment and in the education of children with cardiac disease in the Institute in Teplice, near Hranice, Czechoslovakia.

FROM THE AUTHOR'S SUMMARY.

HEPATIC DISTOMIASIS (FASCIOLIASIS): REPORT OF A CASE IN A CHILD. HANS MOORMAN, Med. Klin. **45**:4 (Jan. 6) 1950.

The patient, a 6 year old girl, was admitted to the hospital with three outstanding symptoms: greatly enlarged, firm, tender liver, anemia and eosinophilia. The serum bilirubin level was not increased above normal. On postmortem examination of the liver purulent cholangitis and pericholangitis were seen, with involvement of the parenchyma. About 25 fully grown large parasites (Fasciola hepatica) were recovered from gallbladder, as well as the extrahepatic and intrahepatic bile ducts. Attention is called to the rarity of fascioliasis in man, in spite of the prevalent possibility of invasion from infected animals, vegetables and fruit.

AMBERG, Rochester, Minn.

HEMAGGLUTININS IN INFECTIOUS MONONUCLEOSIS AND IN SERUM SICKNESS. J. TOMCSIK and H. SCHWARZWEISS, Schweiz. med. Wchnschr. **80**:1 (Jan. 7) 1950.

From the stroma of the red blood corpuscles of sheep four antigens can be extracted. These react with various antibodies. One of these is responsible for the reaction in infectious mononucleosis. One agglutinates sheep corpuscles with human serum after injection of horse serum; another results in the Forssman antibody. These are heteroantibodies, while the fourth, the basis for the Wassermann reaction, is a homologous specific antibody. The procedure may be outlined briefly. The agglutination titer of the patient's serum is determined. The hemagglutinins are absorbed with varying amounts of the different antigens. The hemagglutinin capacity of the serum remaining after absorption is determined. The absorption analysis is of special value in conjunction with the determination of

the heterologous antibody reactions with serum from patients with infectious mononucleosis. For more detail the paper must be consulted.

AMBERG, Rochester, Minn.

CURE OF TETANUS WITH DRAINAGE OF CEREBROSPINAL FLUID. L. SARKADY, Schweiz. med. **80**:106 (Feb. 4) 1950.

Sarkady reports 35 cases of severe tetanus infections, 29 of which were cured by removal of cerebrospinal fluid every day or every second day. The duration of the treatment is not stated. After the removal of the fluid, the wound is excised and cauterized. Antiserum is given prophylactically and after spinal drainage intravenously. Magnesium sulfate is preferred for treatment of the spasms.

AMBERG, Rochester, Minn.

Chronic Infectious Diseases

ONE HUNDRED CASES OF MILIARY AND MENINGEAL TUBERCULOSIS TREATED WITH STREPTOMYCIN. PAUL A. BUNN, Am. J. M. Sc. **216**:286 (Sept.) 1948.

Twenty-five patients with acute miliary tuberculosis and tuberculous meningitis were treated with streptomycin. Fourteen of these patients died within 6 weeks of the onset of treatment without the streptomycin's having exerted any demonstrable effect on their clinical course or on the severity of their lesions. This high percentage of early deaths (56 per cent) cannot logically be attributed to the development of a resistance to streptomycin, and all one can say is that the infection was so overpowering and widespread as to make the drug useless. Veterans Administration Hospitals are, at the moment, exploring the effects of larger doses of therapy with streptomycin and promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) on this type of patient.

Six of the remaining 11 patients died. In 1 of these, streptomycin treatment was without benefit. A decided clinical improvement occurred in the other 5, but it was not maintained despite continued treatment, and death occurred in all 6 six to twenty weeks after the start of therapy. Five are still living, of whom 2 have recently completed a second course of therapy required by a recurrence of their meningitis; these 2 and 2 other patients treated continuously for six months are all doing poorly. The result in only 1 patient of the 25 can be considered a therapeutic success.

Although the end results of streptomycin therapy in this group are unsatisfactory, the ability of the drug to affect the tuberculous lesion has again been demonstrated. The lives of 10 patients were indubitably prolonged by streptomycin treatment and in 8 of these the pulmonary dissemination, visualized on roentgenogram, cleared entirely. The preexisting sources of the dissemination were improved in 7 patients and arrested in 1. As in the group described previous to this, the presence of meningitis in addition to pulmonary dissemination appears to be responsible for the high mortality rate.

It will be observed that no patient receiving less than 189 Gm. of streptomycin intramuscularly or less than 22 intrathecal injections of the drug survived.

HENSKE, Omaha.

TUBERCULOSIS OF THE CHOROID IN A CASE OF MILIARY TUBERCULOSIS TREATED WITH STREPTOMYCIN. J. P. HALBERG, Ann. d'ocul. **181**:485 (Aug.) 1948.

The author reports the case of a 16 year old boy with miliary tuberculosis who showed evidence of miliary tubercles in the choroid of both eyes. He received

247.5 Gm. of streptomycin over a period of four months, with no toxic manifestations. The pulmonary tuberculosis receded rapidly, and the choroidal lesions showed progressive cicatrization. McDonald [Arch. Ophth.].

Treatment of Miliary Tuberculosis and Tuberculous Meningitis with Streptomycin, a Sulfone (Promin®) and Vitamin A. Cesare Cocchi, Riv. clin. pediat. 46:209 (April) 1948.

The results of studies made by the author from December 1946 to April 1948 in the pediatric clinic of Florence, Italy, on the therapy of tuberculous meningitis and miliary tuberculosis with streptomycin, a sulfone and vitamin A are reported. One part of the report represents material presented to the Congress of Internal Medicine held in Rome, Italy, in October 1947; to this data the results obtained up to April 30, 1948 are added. In the first period, December 1946 to July 1947, the technic of small intraspinal and intramuscular doses of streptomycin, together with promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) and vitamin A, was used. Patients who did not die in the first days and whose diagnosis was substantiated by the presence of tuberculosis bacilli in the spinal fluid are reported on. Fifty-five persons with tuberculous meningitis received treatment; 22 were definitely cured without any later effects, returned to their normal occupations and no longer received treatment; recovery in the first patients, who no longer needed treatment, dated from April 1947; all these patients have been cured for more than five months. Repeated checks showed that they not only were clinically cured but also showed normal spinal fluid. Their general condition was excellent. Two are on the road to recovery, 1 still shows signs of radiculitis and partial block; the other has been clinically cured for several months, but the spinal fluid still shows signs of inflammation. Thirty-three have died, the greater number after many months because of relapse and with signs of partial or total block. The daily treatment of these patients was carried out, with but few days' interruption, for ten to twenty days. The greater part of the patients definitely restored to health were cured after relapse and their recovery was obtained, both from the clinical point of view and in regard to the spinal fluid, slowly and with various periods of improvement and setback. None of the 22 patients cured in these two respects showed any further sign of the disease or of relapse.

In the second period, July 1947 to April 1948, 52 patients with tuberculous meningitis received treatment; for this period patients with a dubious diagnosis, without tuberculosis bacilli in the spinal fluid, and patients who died a few hours or a few days after their admission to the clinic were not included. Of 52 patients treated, 20 were definitely cured from the clinical point of view and in regard to the spinal fluid. Three patients died a short while after treatment was started, mostly because of encephalitic symptoms present at the time of their admission to the clinic; 7 are still in the acute phase of the disease but are improving; 17 are clinically cured but the spinal fluid is not completely normal, although showing slow but gradual improvement. There have been no relapses among these last 44 patients.

In this last period, July 1947 to April 1948, the patients were treated as follows: Small doses of streptomycin were given intraspinally (the same as those used in the previous period), that is to say, 1 microgram per kilogram of body weight intraspinally for the adult and older child, with a gradual reduction of the doses in the period of advanced therapy; 2 micrograms per kilogram of body weight intraspinally each day in the small child and 3 micrograms per kilogram of body weight for the infant. The essential difference between the method used in the

first and second period was the continuous, daily intraspinal treatment without interruption for the first thirty, forty and fifty days; in the following interval injections were given every other day as long as the spinal fluid did not become nearly normal. After this, the intraspinal therapy was still further reduced to one treatment every two days, to two weekly and to one weekly, continuing this last for one or two months even though the spinal fluid was normal. Streptomycin was given intramuscularly in the dosage of 0.01 Gm. per kilogram of body weight in three or four daily doses for three to four months until the spinal fluid became normal. The same may be said for the intravenous treatment with promin,* which was given daily in a dose of 3 to 1.5 Gm. according to age. All concomitant therapeutic mediums were used, such as calcium intravenously, vitamin C, lecithin intravenously, blood transfusions and glucose solutions intravenously.

The results obtained in the latter period of treatment, which lowered the mortality of tuberculous meningitis to less than 20 per cent, with a great number of cured patients who did not have later effects or relapses, showed that, compared with the previous data, the fundamental points of successful therapy of tuberculous meningitis consist in the administration of small doses of streptomycin, with promin* and vitamin A, in intraspinal doses daily, and later every two days (but this less frequent treatment must be undertaken only when the spinal fluid tends to become normal). This is certainly the surest way to cure tuberculous meningitis.

In miliary tuberculosis of the lungs the treatment with small doses, as already mentioned, continued for three to four months, and in some cases for many months, always leads to recovery, and the patient is permanently and definitely cured.

FROM THE AUTHOR'S SUMMARY.

RETICULOCYTES AND THE RETICULOCYTIC FORMULA IN VISCERAL LEISHMANIASIS IN CHILDREN. GIACOMO PARRINELLO, Riv. clin. pediat. **46**:364 (June) 1948.

The author studied the behavior of the reticulocytes and the reticulocytic formula in 15 children with visceral leishmaniasis and observed that the reticulocytes increased notably in total numbers, as well as in their percentage in proportion to the total number of red blood cells. The reticulocytic formula showed remarkable flattening with a definite movement toward the left. There was a constant relation between the behavior of the reticulocytic formula of the peripheral blood and the erythroblastic hyperplasia of the bone marrow. No evident relation between the qualitative alterations of the formula and the duration of the disease was noted.

FROM THE AUTHOR'S SUMMARY.

STATISTICS ON 183 PATIENTS WITH TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN, SULFONES AND VITAMIN A. G. PASQUINUCCI, Riv. clin. pediat. **47**:6 (Jan.) 1949.

Statistics are presented on 183 patients with tuberculous meningitis admitted to the Pediatric Clinic of Florence, Italy, from Dec. 11, 1946 to June 30, 1948 and treated with streptomycin, sulfones and vitamin A. The importance of continuous intramuscular and intraspinal therapy until the spinal fluid clears is stressed. Observations are made on the influence of the age of the patient and of an early diagnosis on the results of this therapy.

FROM THE AUTHOR'S SUMMARY.

CHANGES IN THE CEREBROSPINAL FLUID IN THE COURSE OF TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. P. PERITI, G. PASQUINUCCI and C. CALANDI, Riv. clin. pediat. **47**:28 (Jan.) 1949.

A summary is given of the principal concepts on the interpretation of the spinal fluid symptomatology during tuberculous meningitis treated with streptomycin from

observations on more than 200 cases. The behavior of the morphologic elements, of proteins, of chlorides and of the reducing substances in globulin reactions (Pandy, Nonne Apelt, Lange) are stressed.

FROM THE AUTHORS' SUMMARY.

CHANGES IN ALLERGY-IMMUNITY REACTIONS IN PATIENTS WITH TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN (CUTANEOUS REACTIONS TO TUBERCULIN, SEDIMENTATION RATE AND LEUKOCYTIC FORMULA). P. PERITI, G. PASQUINUCCI and A. MILANI-COMPARETTI, Riv. clin. pediat. **47**:41 (Jan.) 1949.

The results obtained in allergy-immunity tests (intradermal reaction, sedimentation rate, leukocytic formula) at the commencement and during treatment with streptomycin are described in 183 patients with tuberculous meningitis treated in the Pediatric Clinic in Florence, Italy. The death rate in patients with a positive reaction to the Mantoux test on admission was well below that observed for patients with negative reactions to the Mantoux test. A positive Mantoux reaction on admission is considered a clear sign of a favorable prognosis, especially for patients between the ages of 2 and 20 years.

FROM THE AUTHORS' SUMMARY.

IMPROVEMENT IN TECHNIC FOR BACTERIOSCOPIC SEARCH FOR THE KOCH BACILLUS (MYCOBACTERIUM TUBERCULOSIS) IN CEREBROSPINAL FLUID. A. MURATORE and G. PASQUINUCCI, Riv. clin. pediat. **47**:60 (Jan.) 1949.

A new method is described for bacterioscopic search for Koch's bacillus (Mycobacterium tuberculosis) in the spinal fluid. On comparison of the results obtained with this method with results of cultural tests made on Petragnani's medium a higher percentage of positive results were obtained with the new method.

FROM THE AUTHORS' SUMMARY.

RESULTS OF DIRECT BACTERIOSCOPIC EXAMINATION OF SPINAL FLUID IN TUBERCULOUS MENINGITIS DURING THE COURSE OF STREPTOMYCIN THERAPY. A. MURATORE and G. PASQUINUCCI, Riv. clin. pediat. **47**:66 (Jan.) 1949.

This is a summary of observations on the behavior of Koch's bacillus (Mycobacterium tuberculosis) in the spinal fluid of more than 200 patients with tuberculous meningitis. The fluid was examined bacterioscopically at the beginning of treatment with streptomycin, during the therapy and in relapses.

FROM THE AUTHORS' SUMMARY.

NEW TECHNIC FOR LOCAL TREATMENT WITH STREPTOMYCIN OF SUPRATENTORIAL ARACHNOIDAL SPACES. G. PASQUINUCCI and A. MILANI-COMPARETTI, Riv. clin. pediat. **47**:77 (Jan.) 1949.

A new technic is described for the introduction of streptomycin into the meningeal spaces of the base and convexity of the cranium. It is especially useful in cases of tuberculous meningitis with spinal fluid block of the spaces over the tentorium.

FROM THE AUTHORS' SUMMARY.

FURTHER OBSERVATIONS ON VARIATIONS IN DIFFUSION OF STREPTOMYCIN DURING THE COURSE OF TUBERCULOUS MENINGITIS. A. MILANI-COMPARETTI, G. PASQUINUCCI and A. ZOLI, Riv. clin. pediat. **47**:86 (Jan.) 1949.

Further observations were made on the "diffusion index" of streptomycin from the lumbar sac to the arachnoidal spaces of the cisterna magna. The authors

observed that changes in the diffusion index are not only a sure and indispensable guide to the treatment of tuberculous meningitis but also show, more sensitively and promptly than the increase in the spinal fluid proteins, the formation of partial blocks in the spinal fluid circulation and the transition of tuberculous meningitis from the exudative to the productive stage.

FROM THE AUTHORS' SUMMARY.

TECHNIC OF LOCAL TREATMENT WITH STREPTOMYCIN OF TUBERCULOUS FOCI IN BONES AND JOINTS, LYMPH NODES AND TESTES. ANTONIO RIGHINI, Riv. clin. pediat. **47**:89 (Jan.) 1949.

A technic is presented for the local treatment with streptomycin of tuberculous foci in the bones and joints, lymph nodes and testes.

FROM THE AUTHOR'S SUMMARY.

BACTERIOSCOPIC DEMONSTRATION OF TUBERCLE BACILLI ON MEMBRANE FILTERS FROM THE CEREBROSPINAL FLUID IN CASES OF TUBERCULOSIS MENINGITIS. CARL-JOACHIM TIETZ and FRITZ HEEPE, Med. Klin. **45**:111 (Jan. 27) 1950.

With a specially constructed apparatus, a membrane, made from nitrocellulose-containing material of 1 to 0.125 sq. cm., can be used. It is recommended to add 10 ml. of cerebrospinal fluid to 2 ml. of 4 per cent sodium citrate solution; later 3 ml. of 50 per cent "antiformin" is added, and the mixture is kept in a water bath at 40 to 50 C. for five to ten minutes. Then 0.1 to 0.5 of 50 per cent sodium thiosulfate solution is added and 6 ml. of a freshly prepared acetic acid-alcohol mixture. The p_H is determined by indicator paper and is adjusted to p_H 5.5 to 6.0. While still warm, the mixture is filtered under negative pressure. While the filtrate is still in the apparatus, the bacteria are stained on the filter membrane with fuchsin and if desired counterstained with methylene blue, brilliant green or chrysoidin. All reagents, including the distilled water, have to be filtered before use through appropriate filters. After drying, the membrane is transferred to a slide cleared with a little xylene and mounted in Canada balsam. The whole procedure requires about one hour. Artefacts may produce difficulties. In 50 of 60 cases of tuberculous meningitis, tubercle bacilli could be found by this method. In 42 of these cases, the disease was of recent origin. The first examination was successful in 26 of these. Once or more frequently repeated examination was necessary in 12 more. The result of the examination could be reported two hours after admission.

AMBERG, Rochester, Minn.

BCG VACCINATION OF NEWBORN INFANTS AND THE EFFECTIVENESS OF VARIOUS METHODS OF VACCINATION. JOHN LIND, Svenska läk.-tidning. **44**:738 (March 28) 1947.

The incidence of tuberculin sensitivity in newborn infants after BCG vaccination in regard to three different methods of administration was studied. The intradermal injection of 0.05 mg. (111 infants) produced tuberculin sensitivity in 86.5 per cent. Injection of 0.10 mg. (215 infants) gave a positive reaction in 95.3 per cent. The scarification method with 20 mg. of BCG vaccine per cubic centimeter (133 infants) resulted in positive reactions in 49.6 per cent. The Rosenthal-Birkhaug multiple puncture method with the same vaccine as with scarification (118 infants) produced positive reactions in 38.1 per cent. The tuberculin tests were performed with 1 mg. of old tuberculin usually three months after vaccination, and the reactions were read after three days.

WALLGREN, Stockholm, Sweden.

BACTERIAL CONTAMINATION OF TUBERCULIN DILUTIONS. ROLF LUNDSTRÖM, Svenska läk.-tidning. **44**:913 (April 18) 1947.

Of 9 infants who were given intradermal tuberculin tests 6 became ill with fever and malaise during the first two days after the injection and displayed on the third day prominent swelling, discoloration and pustule formation at the site of injection. These healed without further complications. The tuberculin was withdrawn from a 1:100 dilution prepared by the state bacteriologic department in glass bottles with a rubber membrane stopper and 0.02 per cent solution of 8-hydroxyquinoline sulfate (chinosol®) as an antiseptic. The tuberculin dilution was two weeks old when used. Bacteriologic examination of the bottle showed gram-negative rods. Later, the bottles of tuberculin were used only one week and no further infections were seen, although 30 per cent of the bottles at that time were found to contain different types of staphylococci, streptococci and other germs.

WALLGREN, Stockholm, Sweden.

FIRST CASE OF TOXOPLASMOSIS DIAGNOSED IN SWEDEN. J. HENNING MAGNUSSON, Svenska läk.-tidning. **44**:1313 (June 13) 1947.

A newborn infant was infected by its mother who had a subclinical toxoplasmotic infection. The disease was diagnosed when the child was 3½ months old. There were calcifications of the choroid plexus, bilateral microphthalmos and mental deficiency. The neutralization reaction was positive in both mother and child. The child survived.

WALLGREN, Stockholm, Sweden.

IS COMPULSORY BCG VACCINATION NECESSARY IN SWEDEN? ARVID WALLGREN, Svenska läk.-tidning. **44**:1545 (July 25) 1947.

In Sweden there is no formal compulsory BCG vaccination as in Norway. The author regards compulsory vaccination as unnecessary because voluntary vaccination is so frequent (annually 200,000 persons are vaccinated, including 130,000 newborn infants) that with continuance of this rate the whole tuberculin-negative population ought to be vaccinated in ten years. Compulsory vaccination is, however, recommended, for conscripts. Informal compulsory vaccination already exists in Sweden for nurses, pupils in infirmary schools, students of medicine, physicians and personnel in hospitals for tuberculous patients.

WALLGREN, Stockholm, Sweden.

CALMETTE VACCINATION AS AN EMERGENCY MEASURE. ARVID WALLGREN, Svenska läk.-tidning. **44**:2241 (Nov. 21) 1947.

A medical health officer was reported to the Swedish State Board of Health by a young woman with pulmonary tuberculosis for not having vaccinated with BCG her 11 and 13 year old sister and brother. The health officer had declined to vaccinate the children because their sick sister did not comply with the requirement of being segregated from them for six weeks before vaccination (six weeks from the time of their last exposure to the sister). The author concludes that it is better in such a case to vaccinate than not to vaccinate, because the injection of the BCG vaccine is not dangerous and may confer immunity if the children by chance were not infected before the incubation period of the vaccine, that is, about six weeks. The reason segregation has been required is to prevent misinterpretation of the failure of the vaccination should virulent infection occur before any BCG immunity has time to be manifested.

WALLGREN, Stockholm, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

SURGICAL TREATMENT OF PATENT DUCTUS ARTERIOSUS. JOHN C. JONES, California Med. **70**:391 (May) 1949.

Since it appears that the diagnosis of patent ductus arteriosus can be made accurately in a high percentage of cases, and as the surgical treatment of this lesion is highly successful with a low mortality and morbidity rate, operation is advisable for all patients with this lesion except those who are 35 years of age or older and who have no progressive cardiac hypertrophy and no incapacitation due to the fistula. The optimum age for operation is 3 years. The vast majority of the patients have a ductus that can be divided, and division has advantages over ligation.

In cases in which patent ductus arteriosus is complicated by subacute bacterial endocarditis, operation should be done following intensive penicillin therapy.

FROM THE AUTHOR'S SUMMARY.

THE DIAGNOSIS AND SURGICAL TREATMENT OF TETRALOGIES. MARY B. OLNEY, California Med. **70**:453 (June) 1949.

Patients with congenital heart disease of the cyanotic type may be presumed to be candidates for surgical treatment if the examination of the heart reveals compatible findings, particularly murmurs characteristic of an interventricular septal defect, overriding aorta and pulmonary stenosis; if the electrocardiogram shows right axis deviation; if the roentgenogram or fluoroscopic study demonstrates decreased pulmonary markings; if iodopyracet (diodrast®) injection shows right ventricular enlargement, a septal defect, overriding of the aorta and small pulmonary arteries.

In some cases some of these criteria may be missing. If there are not definite contraindications, exploratory thoracotomy is indicated for patients with congenital heart disease causing cyanosis.

FROM THE AUTHOR'S SUMMARY.

ACUTE HEMOLYTIC ANEMIA DUE TO NAPHTHALENE POISONING. WOLF W. ZUELZER and LEONARD APT, J. A. M. A. **141**:185 (Sept. 17) 1949.

In 4 instances, children 2 years of age ingested an unknown number of mothballs and acquired severe hemolytic anemia and hemoglobinuria. The condition was duplicated in dogs by giving naphthalene in their food. Differentiation from so-called Lederer's anemia is difficult unless a history of ingestion of naphthalene is specifically elicited.

KIMBALL, Evanston, Ill.

AUREOMYCIN IN STAPHYLOCOCCIC MENINGITIS COMPLICATING SUBARACHNOID HEMORRHAGE IN SICKLE CELL ANEMIA. JOHN R. ALMKLOV and ARILD HANSEN, Pediatrics **3**:764 (June) 1949.

The rare occurrence of a spontaneous subarachnoid hemorrhage in an 11 year old Negro boy with sickle cell anemia is recorded. Of the 8 reported cases 5 have been of children. In the study of sickle cell anemia it is evident there is an increasing awareness of this as well as other neurologic complications.

This patient had Staphylococcus albus meningitis which for twelve days resisted combined penicillin, streptomycin and sulfadiazine therapy. The response to aureomycin given as a sole therapeutic agent was dramatic, and this represents the first reported case of meningitis treated with this drug.

The use of aureomycin as the only antibiotic in this staphylococcic infection seems to have been fortunate in view of the laboratory findings. In vitro studies disclosed that when penicillin and aureomycin or streptomycin and aureomycin were combined the result was a decrease in the effectiveness of either drug against staphylococci.

FROM THE AUTHORS' SUMMARY.

ACUTE ISOLATED MYOCARDITIS: REVIEW OF THE LITERATURE AND REPORT OF A CASE IN A TEN YEAR OLD CHILD. MORTIMER W. WEBER, JANET S. BALDWIN and JOHN W. HALL, Pediatrics **3**:829 (June) 1949.

Acute isolated myocarditis is a relatively rare syndrome of unknown causation, in which the myocardium is the seat of pathologic changes, with complete absence of involvement of the endocardium and pericardium. The main clinical feature is rapid appearance of signs and symptoms of myocardial failure in the absence of past history and present manifestations of rheumatic fever or any other infectious disease known to be associated with myocardial damage. The course is short, usually terminating in death in three days to several months. The disease occurs for the most part in young children or in adults in the third and fourth decades of life. There have been few cases reported in the older child. A case presentation is given of a 10 year old girl who lived for six days after the onset of symptoms. Postmortem observations are included. The diagnosis of acute isolated myocarditis can only be suspected clinically. Final diagnosis can be made by the correlation of gross and microscopic postmortem observations with the clinical features.

FROM THE AUTHORS' SUMMARY.

PHONOCARDIOGRAPHIC DIFFERENTIATION OF THE MURMUR OF MITRAL INSUFFICIENCY FROM SOME COMMONLY HEARD ADVENTITIOUS SOUNDS IN CHILDHOOD. T. N. HARRIS, SIDNEY FRIEDMAN and CARL F. HAUB, Pediatrics **3**:845 (June) 1949.

Phonocardiographic tracings were recorded in children with known insufficiency of the mitral valve, children with a variety of systolic murmurs without a blowing quality and children with no audible cardiac murmurs. The murmurs of valvular insufficiency produced tracings with a completely patternless and disorganized wave form. The other nonblowing murmurs all yielded tracings of uniform sine wave character, regardless of their acoustic quality. Of these, the majority were "twanging-string" murmurs, the loudest of these with a distinct buzzing quality; the others were "snorting," "scraping" or "grating" in quality. Clinical observations indicated that these nonblowing murmurs were not indicative of cardiac disease. The murmurs of mitral insufficiency were significantly longer than the nonpathologic murmurs, but the latter showed, on the average, fully as great amplitude on the tracings. Physical and clinical implications of these observations are discussed.

FROM THE AUTHORS' SUMMARY.

CYCLIC NEUTROPENIA IN AN INFANT. STANFORD BORNE, Pediatrics **4**:70 (July) 1949.

Repeated episodes of neutropenia, lymphocytosis, infection and fever were observed in a 2½ year old infant since the age of 5 months. The cycles recurred every three weeks and were initiated by the rapid and usually complete disappearance of the neutrophils; this neutropenia was accompanied with a slight monocytosis and leukopenia, a decided relative and a slight absolute rise in lymphocytes and the appearance of a few atypical forms of the latter cells. Two or three

days later the patient always showed an acute infection, fever and lassitude. Clinical recovery took place in one week and hematologic recovery in two weeks. Physical examination during her asymptomatic periods gave essentially normal results.

A rise in urinary estrogens and a positive reaction to a test with chorionic gonadotropin just preceding the neutropenia suggested a causal relationship between a female endocrine disturbance and the hematologic cycles. Six sternal marrow biopsy specimens showed a changing leukocyte pattern; but failed to establish a diagnosis of leukemia. Laboratory tests showed no abnormality. Roentgenograms revealed a ground-glass appearance of the long bones and widening of the medullary cavity but normal carpal and tarsal development.

Diethylstilbestrol and progesterone therapy and a whole blood transfusion apparently suppressed the neutrophils. Administration of sulfadiazine, penicillin and streptomycin helped control the infections but did not alter the course of illness. Folic acid, pentnucleotide® (a preparation of the sodium salts of pentose nucleotides), pyridoxine hydrochloride and autogenous vaccine therapy had no demonstrable effect.

FROM THE AUTHOR'S SUMMARY.

INFLUENCE OF SEX FACTORS IN TRANSFUSION REACTIONS. A. HUSTIN and R. REMY, Presse méd. **54**:728 (Nov. 2) 1946.

The authors advise the use of male donors exclusively for transfusions. In a series of 864 cases, reactions were more frequent when the donor was female. The highest percentage of reactions (17.3 per cent) was in cases in which both the donor and the recipient were female, the lowest (5.3 per cent) in cases in which both the donor and the recipient were male. Female donors produced reactions in 6.3 per cent of male recipients, and male donors produced reactions in 9.1 per cent of female recipients.

DAFFINEE, Melrose, Mass.

MYELOGRAMS AND PATHOGENESIS IN ACUTE HEMOLYTIC ANEMIA FROM FAVISM. FRANCESCO PECORELLA, Arch. ital. di pediat. e. puericol. **11**:434, 1947.

The author describes 3 cases of favism, which occurred in the province of Palermo, Italy, in children 32, 10 and 14 months old. The first 2 children recovered, but the third died. After mentioning the uncertainty of the pathogenesis of favism and the insufficient researches made on the bone marrow in this disease, he relates the results obtained on myelograms executed with medullary material extracted for biopsy in the different periods of illness. In the study of the pathogenesis of favism he also made various biologic and serologic tests.

The myelograms showed granuloblastic and chiefly erythroblastic hyperplasia, with a considerable degree of anaplasia and a conspicuous prevalence of cytoevolutive phenomena over cytoreproductive ones. Passage into circulation of the less immature cellular elements was rapid, and several rare histoid elements with erythroblastic tendencies were present. Typically megaloblastic elements were absent.

The curves for erythroblastic and leukoblastic maturation appeared generally displaced to the left and they were of a slow evolutive type. The indexes of erythroblastic and leukoblastic maturation were decreased, and the karyokinetic elements in both the red and the white cell groups were less numerous than normal. The karyologic curves were, as Fieschi termed them, of a regenerative, stimulated type.

The intradermal reaction with an extract of fresh broad beans gave a positive result in 2 cases of favism; positive results were likewise obtained in 7 cases of

passive transmission by the Prausnitz and Küstner method, while the Lehner and Raika process gave a negative result with 3 rabbits. The search for autohemolysins always gave negative results.

FROM THE AUTHOR'S SUMMARY.

INTERPRETATION OF MYELOGRAMS OF NORMAL SARDINIAN BABIES. G. MACCIOTTA and A. LEONE, Arch. ital. pediat. puericolt. **12**:185, 1948.

The features of the myelograms of 50 normal children 1 month to 10 years of age, certified to be of Sardinian origin, which were made to establish whether environmental factors acting through preceding generations can influence hematopoiesis, are described by the authors. The present research follows previous works partially published from their school. A comparison is made of these findings with similar ones, already published, concerning the area of Bologna, Milan and Pavia, with reference to children of the same age and to adults. Lymphocytic cells average from 0.5 to 0.8 per cent, which is not so high as the figures shown on the previous myelograms. Scantiness of myelocytic cells, with a sharp rise from the most immature to mature cells (metamyelocytes and young granular leukocytes), is typical. Values for hemocytoblasts are noted to be reduced on comparison with the previous myelograms. For adults the values are closer to but higher than Fieschi's data.

Myeloblasts and promyelocytes in the first two triennial periods are equivalent, but myeloblasts prevail in the third triennial period. Scantiness of myelocytes is attributed to the rapid evolution toward mature cells, which appear to be more numerous than in other myelograms. Eosinophilia is obviously reduced.

Curves for maturation, calculated with Pontoni's method, rise gradually for myelocytes and sharply in the later stages, while in the curves for Bologna and Pavia the rise was sharper in preceding periods. The ratio of myeloblasts to granular leukocytes expressing evolutive dispersion is, according to Cagliari's findings, 1:20, as against 1:16.5 for Bologna, 1:8.2 for Pavia and 1:2.4 for Milan for the first three years. The difference is reduced in later periods and almost disappears. Erythroblasts are 30 per cent of the red corpuscles in the first triennial period, about 25 per cent in the second and third, with scant variation from the previous myelograms. Increased basophilia and eosinophilia in the curves of maturation become more obvious. These curves are slowed up by inadequate evolutive stimulation or increased inhibition. Mitotic curves show a reduced activity for the first three years of life as compared with the figures for Pavia, as given by Dordi, and low prophases, high metaphases and intermediate telephases are noted for granulocytes, similar to those in the curves for adults.

The differences in the findings for the various areas and their importance in the evaluation of pathologic conditions are discussed by the authors.

FROM THE AUTHORS' SUMMARY.

THE ERYTHROCYTIC RESISTANCE TO SAPONIN IN MOTHER AND FETUS. A. GENTILI and G. FASCIONE, Arch. ital. pediat. puericolt. **12**:222, 1948.

The authors used the method of Gigli to study the erythrocytic resistance to saponin in fetal and maternal blood. They determined its minimal (E_1), mean (E_2) and maximal (E_3) resistances. They found that the erythrocytic resistance to saponin is higher in the mother than in the fetus, with more sensible differences for E_1 and E_3.

The authors made the interesting observation that erythrocytic resistance to saponin in women at the end of pregnancy, and in the fetus, is highly decreased

as compared with that of healthy adults, even though an increase in the resistance to saponin was expected because in women at the end of pregnancy the existence of hypercholesteremia has been demonstrated. In the fetus, the decrease in the erythrocytic resistance to saponin does not appear proportionate to the decrease in cholesteremia.

The resistance of the red blood cells to the hemolytic action of saponin does not depend, therefore, only on their cholesterol content, or on that of the blood serum (the protective action of which has been demonstrated), but on some other factors that have the capacity in particular conditions (as in the ones studied by the authors) to cancel the antihemolytic action of cholesterol. The authors intend to investigate the action of such factors and to try to find an explanation for the facts they have pointed out. Such an investigation may disclose completely new views on the functional aspects of the red blood cell (or of the blood serum in relation to its protective action on red blood cells).

FROM THE AUTHORS' SUMMARY.

ERYTHROCYTIC FRAGILITY OF NORMAL BABIES AS DETERMINED BY THE METHOD OF SIMMEL. SALVATORE CORBO, Arch. ital. pediat. puericolt. **12**:246, 1948.

Blood cell fragility was determined in 42 normal children, 1 month to 12 years of age, by means of the Simmel method and with the use of freshly prepared solutions. Children in the first month of life were excluded from the study because of the complex behavior of the blood cell fragility at this period.

The mean percentage values for hemolysis in each sodium chloride solution are:

Solutions, % NaCl.....	0.7	0.6	0.5	0.4	0.3	0.2
Hemolysis, %.....	0.50	17.08	69.01	94.27	99.18	99.93

These average figures were obtained from data varying greatly for the first solutions and much less so for the last ones. The resulting values, taken by the author as normal for children, agree with those found by Silvestroni and Bianco in normal adults.

FROM THE AUTHOR'S SUMMARY.

SULFONAMIDE HEMOPATHIES. CRISTINA VIVES BERDÓN, Bol. méd. d. hosp. inf. Mexico **4**:283 (May-June) 1947.

The author analyzes in a general manner the alterations observed in the blood of patients treated with sulfonamide compounds and draws the following conclusions:

1. Frequent examinations of the blood during treatment with sulfonamide drugs are important in order to control any alteration in its elements.

2. These reactions were seldom seen in our material, but they must always be kept in mind because of their gravity and the possibility of relapse when the drug or a similar compound is given again. In such cases, the patient's tolerance for the drug may be tested by giving small doses of 0.06 to 0.12 Gm and waiting twelve hours for the appearance of toxic manifestations, in which case the small doses are repeated.

3. The hemopathies were seen with greater frequency in children and were caused mainly by sulfanilamide and sulfapyridine, although other sulfonamide drugs were also responsible for such a picture. Granulocytopenia and panmyelophthisis occupy the first place respectively in frequency and gravity. Leukocytosis is more seldom seen and is less serious.

One must remember that the best way to avoid, as far as possible, the appearance of these pictures is to use sulfonamide compounds only when there

is a precise indication; doses should not be too large; treatment with them should not be insisted on once the drugs have proved inefficacious. Divided doses should be given, and other medications excluded. One must also inquire whether any reactions resulted from previous treatments with these drugs.

Generally speaking, these are the rules that must be followed for the successful administration of sulfonamide drugs.

FROM THE AUTHOR'S SUMMARY.

LUTEMBACHER'S DISEASE. SAMUEL BERBER G., Bol. méd. d. hosp. inf. Mexico **4**:339 (May-June) 1947.

One case of Lutembacher's disease (mitral stenosis with patent foramen ovale) is presented. It is considered to be of interest to the pediatrician recalling the occasional congenital basis for mitral stenosis.

A review of the history and several observations about clinical signs, prognosis and treatment are included.

This case has some unexplained anomalies: aortic atheromatosis, with widening of the vessel, and an atypical electrocardiogram without the evidence of right ventricular strain.

FROM THE AUTHOR'S SUMMARY.

Diseases of Nose, Throat and Ear

GAMMA GLOBULIN IN RELATION TO INFECTIONS OF THE RESPIRATORY TRACT. WILLIAM J. HITSCHLER, FRANKLIN L. RUTBERG and JOSEPH STOKES JR., Arch. Otolaryng. **48**:527 (Nov.) 1948.

The instillation of a few drops of human serum immune globulin had no effect on the duration and severity of the common cold in the children studied at an orphanage. The longer duration of the common colds in those children who still had their tonsils and adenoids was not highly significant statistically.

KIMBALL, Evanston, Ill.

THE PHYSICIAN'S RESPONSIBILITY TOWARD THE HARD-OF-HEARING AND DEAFENED. FRANCIS L. LEDERER, RICHARD E. MARCUS and ARNOLD A. GROSSMAN, Illinois M. J. **95**:269 (May) 1949.

The greatest advance in the treatment of the deafened has come in the integration of the services of those various specialized fields and agencies that have concerned themselves for years past with hearing-handicapped people. Some hearing-handicapped patients will gravitate directly to rehabilitation hearing centers, but by far the greater majority will come to the family physician. If the physician will give optimistic and sympathetic counsel, the patient can be directed into legitimate, scientific, medical channels, in which his hearing defect can be diagnosed and proper treatment instituted.

Three groups of hearing-handicapped patients will come to the physician's office: 1. The infant and the preschool child. The mother should be told that if her child be found deaf his future education can be assured by the many facilities in the state of Illinois conducted expressly for the hearing-handicapped child. 2. The school child. In Illinois, of 200,000 known handicapped children, an estimated 50,000 have hearing defects. In a recent survey of 21,000 children in Will County, approximately 7 per cent were found to have significant hearing defects. It is within this group of school children that the most important work for the detection, improvement, conservation and rehabilitation can be realized. Since the physician is a key figure in any health program, it is his responsibility to under-

stand and encourage carefully planned and scientifically conducted hearing surveys in his community. 3. The adult. All these people need help of a very special kind.

BARBOUR, Peoria, Ill.

THE PREVALENCE OF COLDS IN NURSERY SCHOOL CHILDREN AND NON-NURSERY SCHOOL CHILDREN. ISABELLE DIEHL, J. Pediat. **34**:52 (Jan.) 1949.

Children who attended a nursery school had no more colds than those who did not attend. Fifty-one children were observed from January to April. The diet and the number of persons in the home had nothing to do with the prevalence of colds. As the mean temperature of the community rose, the prevalence of colds diminished.

MACDONALD, Pittsburgh.

STREPTOMYCIN IN THE TREATMENT OF HEMOPHILUS INFLUENZAE LARYNGOTRACHEOBRONCHITIS. C. O. TERRELL JR. and CARL S. HOAR, J. Pediat. **34**:139 (Feb.) 1949.

Four patients with tracheobronchitis due to Hemophilus influenzae were treated with streptomycin. The results were excellent. All young infants with this disease should be given streptomycin until throat cultures indicate its withdrawal.

MACDONALD, Pittsburgh.

TRACHEAL TUMORS IN INFANTS AND CHILDREN. JOSEPH G. GILBERT, BENJAMIN KAUFMAN and LAURENCE A. MAZZARELLA, J. Pediat. **35**:63 (July) 1949.

Tracheal tumors in infants and children are usually papillomas (56 per cent), fibromas (21.9 per cent) or angiomas (9 per cent). Malignant tumors (sarcomas) are rare. Gilbert and his colleagues report 2 cases of angioma of the trachea. This makes a total of 41 tracheal tumors in infants and children reported in the literature.

MACDONALD, Pittsburgh.

THE ROLE OF VIRUS INFECTIONS IN THE ETIOLOGY OF SEROUS OTITIS MEDIA. HAROLD G. TOBEY, Laryngoscope **59**:35 (Jan.) 1949.

The incidence of secretory otitis media has increased greatly in recent years. There must be other causes than that of mechanical obstruction of the eustachian tube; in fact, obstruction may have little to do with the condition. Politzer said that the discharging of fluid into the tympanic cavity was due mostly to inflammation of the mucous membrane of the middle ear. Some years ago such inflammation resulted in severe acute otitis media and often mastoiditis; now the insidous mild secretory otitis results. Chemotherapy cannot completely account for this change; rather, an avirulent bacterium or a virus is thought to be present.

Symptoms, signs and stages of the disease are described. Politzerization may clear up the condition, or myringotomy, sometimes repeated, may be necessary. In some cases the cells of the mastoid process become involved, necessitating their removal. The occurrence and importance of secretory otitis media should not be overlooked.

HITSCHLER, Philadelphia [ARCH. OTLARYNG.].

POTENTIAL HAZARDS FROM RADIATION TREATMENT OF HYPERTROPHIED LYMPHOID TISSUE IN THE NASOPHARYNX. LAURENCE L. ROBBINS and MILFORD D. SCHULZ, Laryngoscope **59**:147 (Feb.) 1949.

Untoward effects of roentgen ray and radium treatment may not appear for years. Not enough time has passed since the widespread use of the nasopharyngeal

radium applicator to be certain that such effects will not appear in the future. Harm has resulted from even an erythema dose, and this dose in some cases is less than that used in the nasopharynx. Furthermore, it is difficult to determine the exact amount of radiation which reaches the tissues from the applicator. Because of these potential dangers, the operator is warned not to use this means of therapy without due consideration.

HITSCHLER, Philadelphia [ARCH. OTOLARYNG.].

POSTOPERATIVE TONSIL BLEEDING: STUDIES OF THE ETIOLOGY, PREVENTION AND MANAGEMENT. H. GRANT PRESTON, Laryngoscope **59**:251 (March) 1949.

Preston comprehensively discusses tonsillar bleeding, its prevention and control. The postoperative use of vitamin K greatly reduces the incidence of hemorrhage. Ascorbic acid may also be useful. On the other hand, the use of large amounts of acetylsalicylic acid or of gum containing this agent or undue operative trauma may increase the likelihood of this complication. Many other factors are discussed.

HITSCHLER, Philadelphia [ARCH. OTOLARYNG.].

REHABILITATION OF HARD OF HEARING CHILDREN: A SUMMARY OF THE LAWS AND AN ANALYSIS OF THE SCHOOL TESTING PROGRAM IN NEW YORK STATE. GEORGE J. RIGHTER and PAULINE K. WINKLER, New York State J. Med. **48**:83 (Jan. 1) 1948.

Total deafness is usually discovered early in childhood. Education, including tuition and maintenance, for the unfortunate patients is provided by six institutions in the Empire State. Those who are hard of hearing (not totally deaf), state the authors, "can be completely rehabilitated if all means at our disposal are used." Education and the application of existing laws facilitate the desired end.

A summary of existing laws indicates that four acts are in operation: 1. The Reporting Act provides that all physicians, nurses, parents and guardians must report hearing impairment in children under 6 years of age to the State Commissioner of Health in order that the child may be properly oriented and cared for. 2. The Audiometer Act provides that all school children must have an audiometer test at least once each year. Thus, poor hearing may be discovered promptly. The state supplies a booklet of detailed instructions for testers. If there is a 9 decibel loss a test with the pure tone audiometer is required; 10 decibel loss recorded with the pure tone audiometer calls for examination by an otologist, and a 20 decibel loss is reportable to the Commissioner of Health. This applies to all cities save New York, Buffalo and Rochester! 3. The Education Act provides for transportation to school, a visiting teacher in the home and special classes. 4. The Rehabilitation Act defines a handicapped person as one who is incapacitated, from whatever cause, for earning a living. Such a person may become a ward of the state if he is not too old or helpless, mentally diseased or under 14 years old (the employment age). All other persons over 14 who have a physical defect because of which they are totally or partially disabled may apply for aid or advice. The Advisory Commission may arrange for treatment leading to rehabilitation except for those who are eligible under the Workmen's Compensation Law. The state may provide the cost of maintenance during actual training and transportation, but the amount must not exceed $15 a week! Training courses under employers are paid for by the state, and books and tools may be so provided.

Statistics of the Conservation of Hearing Department of the Division of Health and Physical Education of the State Education Department give the total number of students, exclusive of those in the three cities mentioned, as 707,767 during the school year 1944-1945. Of these students, 65.3 per cent received the audiometer test in groups. Pupils recommended for special training numbered 91.2 per cent, but not all took advantage of the opportunity. There are Conservation of Hearing classes in four cities: Albany, Schenectady, Gloversville and Syracuse. The charge for tuition is set for nonresident students by the local school superintendent. In addition to these four classes, twenty-eight communities offer classes in lip reading. All but six of these are in the metropolitan area, including Long Island and Westchester County. The six others are located in Auburn, Binghamton, Ithaca, Olean, Utica and Watertown. Statistics for the period 1944-1945 show that 1 child in every 53 of the 462,304 tested had a loss of 15 decibels or more, that 1 in 500 was recommended for special education and that 1 of every 607 received it. It is notable that the Catskill and Adirondack areas have no rehabilitation facilities whatsoever.

Certain clinics for conservation of hearing in approved hospitals serve to assist in the classification of children and in their direction toward the sources from which they may expect help. Two types of educational service are still needed: (1) conservation of hearing classes in public schools, with full time teachers in large cities and towns, and (2) lip-reading and speech correction classes in areas where there are no conservation of hearing classes. There is a need for specially qualified teachers for the deafened, and colleges and universities throughout the state have a responsibility to offer training for such teachers.

VOORHEES, New York [ARCH. OTOLARYNG.].

ADVISING PARENTS OF EARLY STUTTERERS. SPENCER F. BROWN, Pediatrics **4**:170 (Aug.) 1949.

A brief review of a number of research studies on stuttering is presented. Physiologic and biochemical differences between stutterers and nonstutterers were found to be slight or absent. The increased muscle tension and the startle reaction pattern of most adult stutterers explain the differences noted.

Research has shown that repetition is normally present in the speech of preschool children. Parents or other persons may mistakenly diagnose this repetition as stuttering. Such a misevaluation leads to unwarranted concern over the child's speech and disapproval of his repetitions. In a vain effort to eliminate nonfluency, the child develops tension which increases the frequency and duration of the moments of nonfluency. Therapy for the beginning stutterer is directed at the parents and takes the form of education concerning realistic standards for the speech of preschool children generally and reassurance of the essential normality of their own child's speech.

FROM THE AUTHOR'S SUMMARY.

"OPEN" ENDOTRACHEAL ANAESTHESIA FOR TONSILLECTOMY AND ADENOIDECTOMY IN CHILDREN, WITH A NOTE ON PRE-OPERATIVE MEDICATION. BLUMY SEGAL, South African M. J. **23**:514 (June 25) 1949.

A technic of endotracheal anesthesia using an open T tube is described. No expiratory valve or rebreathing bag is employed. The method gives highly satisfactory results and is recommended as a routine procedure for this operation.

MCGUIGAN, Evanston, Ill.

Diseases of Lungs, Pleura and Mediastinum

CONGENITAL CYSTIC DISEASE OF THE LUNG IN INFANTS AND IN CHILDREN. MARK M. RAVITCH and JANET B. HARDY, Arch. Surg. **59**:1 (July) 1949.

This condition, which has been considered extremely rare, is described by the authors in 12 patients. The patients were treated in a single hospital within the preceding five years. The occurrence of the disease in newborn infants establishes it as congenital. The embryonic mechanism and the time of formation of the defect have not been established. The clinical manifestations varied, depending on the location and the size of the cysts. Chronic cough was the most constant symptom. Six of the patients had repeated bouts of pulmonary infection severe enough to be called pneumonia. Dyspnea, constant or in episodes, was observed in all patients. Eleven of the 12 patients were successively treated by surgical removal of the involved area of lung (6 had single lobectomy; 4, lobectomies of two adjacent lobes, and 1, pneumonectomy). The single death from pneumonia occurred in an infant of 8 months for whom operation had been deferred and was not performed. Resection of the cyst or of the cyst-bearing segment of lung is the recommended treatment.

KAISER, Rochester, N. Y.

DETECTION OF VARIOUS CHEST LESIONS BY MASS X-RAY SURVEY. DAN MORSE, Illinois M. J. **95**:279 (May) 1949.

Nearly 60,000 roentgenograms were taken in a roentgenologic survey conducted in Peoria in 1947. The highest total incidence of cases of tuberculosis and other pulmonary diseases was in persons who are sick, such as patients admitted to hospitals, people attending a clinic, persons on relief and those who are contacts of patients with active disease. Two hundred and twelve cases of tuberculosis were found. Of these 212 cases, the disease was considered active in 31, classified as questionably active in 51 and thought to be arrested in 130. Over 900 roentgenograms of the chest with significant abnormalities other than tuberculosis were discovered in the survey.

BARBOUR, Peoria, Ill.

PULMONARY EMBOLISM IN CHILDHOOD. GEORGE F. STEVENSON and FERN L. STEVENSON, J. Pediat. **34**:62 (Jan.) 1949.

The case reported was that of a 9 year old boy. The embolus was secondary to a thrombophlebitis in the femoral and iliac veins and the inferior vena cava.

MACDONALD, Pittsburgh.

PULMONARY GANGRENE IN A CHILD FOLLOWING ASPIRATION OF TIMOTHY GRASS. D. JOSEPH JUDGE, E. CLARENCE RICE and EDGAR W. DAVID, J. Pediat. **34**:87 (Jan.) 1949.

Pulmonary gangrene and death followed aspiration of timothy grass by a 21 month old girl.

MACDONALD, Pittsburgh.

PNEUMONIA IN INFANCY CAUSED BY FRIEDLÄNDER'S BACILLUS. BRUCE F. GROTTS, J. Pediat. **34**:174 (Feb.) 1949.

Throat cultures taken from 7 patients with atypical pneumonia showed pure growths of Klebsiella pneumoniae. In all cases the disease had an insidious onset, with cough and vomiting and/or diarrhea. Streptomycin was the most effective therapy.

MACDONALD, Pittsburgh.

BRONCHIECTASIS IN CHILDHOOD: II. AETIOLOGY AND PATHOGENESIS, INCLUDING A SURVEY OF TWO HUNDRED AND SEVENTY-TWO CASES OF DOUBTFUL IRREVERSIBLE BRONCHIECTASIS. C. ELAINE FIELD, Pediatrics 4:231 (Aug.) 1949.

Nonaeration of alveoli is a feature common to the childhood illnesses predisposing to bronchiectasis and is regarded as the important factor in the causation of the disease, infection playing a subsidiary part. Pulmonary collapse is, therefore, regarded as a prebronchiectatic state, and in order to assess its importance two groups of cases were studied: (1) 272 cases of pulmonary collapse, and (2) 99 cases in which the diagnosis of bronchiectasis was doubtful at first examination.

Pulmonary collapse was seen most frequently in the middle lobe of the right lung and the lower lobe of the left lung. It was usually persistent in the upper lobe of the left lung but frequently the lower lobe of the right lung reexpanded. The duration of cough, according to the history, was commonly three months or less in cases of pulmonary collapse in which reexpansion occurred, in contrast to the long history of two years or more in the majority of cases in which bronchiectasis developed.

Of the 272 cases of pulmonary collapse, reexpansion took place in only 157 without permanent bronchiectatic changes. It was not uncommon, however, to find temporary bronchial dilatation in this group, the bronchi returning to normal caliber when the collapsed lung reexpanded—a condition described as reversible bronchiectasis.

The treatment recommended for pulmonary collapse includes steam inhalations, postural drainage and breathing exercises. Unless the presence of a foreign body is suspected, immediate bronchoscopy is no longer considered necessary. No significant difference in the incidence of reexpansion of the lung was noted between the patients treated with bronchoscopy and those treated without.

Ninety-nine cases were classified as of doubtful bronchiectasis when first seen. Of these, 47.5 per cent included asthma, a disease frequently difficult to differentiate from bronchiectasis. In 40 of the 99 cases true irreversible bronchiectasis has now developed after a period of three or more years. It was necessary to observe cases showing doubtful bronchial dilatation over a period of years, the bronchograms being repeated at intervals in order to identify the permanently diseased parts.

FROM THE AUTHOR'S SUMMARY.

PRIMARY ATYPICAL PNEUMONIA. J. C. GERRITS, Nederl. tijdschr. v. geneesk. 92:22 (Jan. 3) 1948.

Primary atypical pneumonia was observed in 7 patients. The symptoms were slightly elevated temperature, coughing, anorexia and sweating during the night. The diagnosis was made on the basis of the roentgenologic findings and the positive reaction in the cold agglutination test. In one family 3 members fell ill with identical complaints at about the same time; 1 of them had a positive reaction to the cold agglutination test. In none of these patients, however, were changes seen on the roentgenograms. These observations are in accordance with the results obtained in the investigations carried out on volunteers. It was possible to transmit the infection; the test persons had a mild attack only and there were no changes on the roentgenogram.

The titer of the cold agglutination test in healthy men and in patients with other types of inflammation localized in the lungs varied but never exceeded 1:64. A titer of 1:128 is therefore considered of diagnostic value; a rising titer at the beginning of reconvalescence is a significant diagnostic symptom.

In 3 patients atelectasis of the middle lobe of the lung was observed. This was best demonstrated on the transverse roentgenogram. In the 7 patients from Amsterdam the disease ran a mild course. Generally patients with these symptoms will be treated at home and a diagnosis of influenza will be made. It is therefore possible that the primary atypical pneumonia is more frequent in the Netherlands than hitherto has been assumed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE PATHOLOGY OF EPIDEMIC HEPATITIS. TRACY B. MALLORY, J. A. M. A. **134**:655 (June 21) 1947.

The pathologic aspects of fatal and nonfatal hepatitis were compared on the basis of a survey of 296 autopsy reports and 160 biopsies from 137 cases of nonfatal disease.

Epidemic hepatitis, in either fatal or nonfatal form, is characterized pathologically by the simultaneous occurrence of inflammatory and degenerative changes in the hepatic parenchyma. In fatal cases the degeneration takes the form of massive autolytic necrosis, which in some areas may be followed by extensive regeneration. In benign cases massive necrosis is seen only exceptionally, whereas acidophilic coagulative necrosis of individual cells is constantly present. Other changes found in the progressive stage of the disease are disorganization of the lobular pattern, focal intralobular collections of inflammatory cells and active regeneration of the cells of the liver. All these factors are present in the prodromal period of the disease before jaundice becomes apparent, and many of them may persist for weeks after it has disappeared. Evidence is presented that acute epidemic hepatitis with histologically characteristic involvement of the liver may run its course without the development of clinical jaundice.

FROM THE AUTHOR'S SUMMARY.

HIRSCHSPRUNG'S DISEASE: A NEW CONCEPT OF THE ETIOLOGY; OPERATIVE RESULTS IN THIRTY-FOUR PATIENTS. ORVAR SWANSON, HAROLD F. RHEINLANDER and ISRAEL DIAMOND, New England J. Med. **241**:551 (Oct. 13) 1949.

Swanson and associates summarize the many theories for the cause of congenital megacolon under four headings: namely, that the lesion is due to (1) a congenital lesion in the dilated colon, (2) the results of actual mechanical obstruction, (3) an infection, such as colitis, and (4) neurogenic imbalance.

Various methods of treatment are grouped as follows under three headings: (1) medical management, (2) surgical resection of the involved bowel, either in whole or in part, and (3) section of the sympathetic pathways to all or part of the colon. These methods are more fully described.

The authors offer a new concept of the etiology of Hirschsprung's disease based on their two cited articles and the roentgenologic evidence accumulated by Neuhauser of a narrow rectosigmoid distal to the dilated sigmoid. Special measures are necessary to demonstrate this abnormal area, but when it is found and the rectum and rectosigmoid are resected by technics which spare the anal sphincter, cure has been prompt and complete in 33 of the 34 patients followed.

Studies were done on the peristaltic wave progression patterns of normal subjects and of 8 patients with Hirschsprung's disease. In the former, strong waves progressed from the transverse colon to the anus. In the latter, the waves did not enter the narrowed distal segments. The defect was considered sufficient to produce chronic obstruction, especially since the defective area was identical

with the narrowed bowel seen on roentgenograms. It is suggested that this defect can be correlated with the finding of absence of ganglion cells in areas of the rectosigmoid.

WHEELOCK, Denver.

FARBER'S TEST IN THE DIAGNOSIS OF CONGENITAL INTESTINAL ATRESIA. NORMAN C. WOODY, New Orleans M. & S. J. **100**:273 (Dec.) 1947.

Farber's test provides a simple and valuable means of determining the presence of congenital atresia of the intestines. The test was not done in 23 patients seen between 1937 and 1946, and the correct diagnosis was made for 7. In 1946-1947, 24 patients were seen and the correct diagnosis was made for 23 after using Farber's test. Woody is of the opinion that the test should be carried out routinely in the first forty-eight hours of life when there is any suspicion of gastrointestinal malfunction.

McGUIGAN, Evanston, Ill.

DISTURBANCES OF WATER AND ELECTROLYTES IN INFANTILE DIARRHEA. DANIEL C. DARROW, EDWARD L. PRATT, JAMES FLETT JR., ALICE H. GAMBLE and HILDA F. WIESE, Pediatrics **3**:129 (Feb.) 1949.

Average deficits per kilogram of body weight in severe dehydration due to diarrhea are —125 Gm. of water, 9.2 millimoles of chloride, 9.5 millimoles of sodium and 10.4 millimoles of potassium. These figures may be about 10 per cent too high for water, sodium and chloride because of overexpansion of extracellular fluids in some cases.

These findings, especially the approximately equal retentions of sodium and chloride during recovery, indicate that: 1. Intracellular sodium is slightly high during dehydration in many infants. 2. Administration of sodium chloride without sodium bicarbonate should suffice to restore all deficits of sodium and chloride. 3. Acidosis is explained chiefly by a deficit of potassium which leads to the transfer of extracellular sodium in the cells during dehydration. 4. Fluids used to replace deficits of water and electrolyte in diarrhea should contain potassium, as well as sodium and chloride. 5. Administration of sodium bicarbonate without potassium salts so as to restore rapidly the concentration of serum bicarbonate in acidosis is likely to aggravate the abnormality in cellular composition and may produce alkalosis and a low concentration of potassium in the serum. Losses of water as sweat are frequently 50 cc. per kilogram of body weight per day; the maximum amount measured was 100 cc. Losses of water in stools are frequently 50 cc. per kilogram of body weight per day; the maximum measured was 85 cc. Losses of nitrogen are rapidly replaced when milk feedings are instituted, even at low caloric intakes. In the development of dehydration, losses of water in sweat are quantitatively as important as losses in stools. The relation of these observations to the treatment of infantile diarrhea is discussed.

FROM THE AUTHORS' SUMMARY.

SUCCESSFUL REMOVAL OF HEMANGIOMA OF THE LIVER IN AN INFANT. THURMAN SHULLER, JOSEPH L. ROSENZWEIG and JAMES B. AREY, Pediatrics **3**:328 (March) 1949.

The successful surgical removal of a benign hemangioma of the liver in a child 22 days old is reported. The authors cite similar cases of 56 persons, previously reported on, the youngest patient being 6 years old. The important fact was the presence of a "silent" mass in the upper part of the abdomen; laboratory data revealed no outstanding abnormalities. Roentgenographic studies showed a mass

in the upper right quadrant which displaced the colon downward and to the left. The diagnosis was confirmed only after histologic study. Because of the impossibility of making a sure preoperative diagnosis and because of the obvious danger in delay, the authors advocate early surgical exploration and removal of such tumors.

FROM THE AUTHORS' SUMMARY.

THERAPY AND PROGNOSIS OF FIBROCYSTIC DISEASE OF THE PANCREAS. D. H. ANDERSEN, Pediatrics **3**:406 (April) 1949.

The origin of the respiratory lesion in fibrocystic disease of the pancreas is discussed, with a summary of the congenital and nutritional hypotheses. There is no morphologic evidence that a specific congenital abnormality exists in the bronchi or in their secretion. The microscopic appearance of the mucus does not resemble that of the contents of the pancreatic ducts but does resemble the mucus seen in some other clinical conditions, notably asthma. A physiologic congenital abnormality of the bronchi is possible but unproved. Evidence is presented that dietary therapy improves the growth curves of infants whose condition is diagnosed and treated prior to infection. The absorption of vitamin A, and presumably of other fat-soluble specific substances, is affected by diet. A series of 22 patients with fibrocystic disease without clinical evidence of respiratory infection is reported on. Twenty-one of these were first seen after penicillin became available but only 11 received it. The majority of the 22 patients was started on dietary therapy before a cough had been present for as long as two months. This record is presented as evidence in favor of a nutritional factor in the origin of the respiratory infection.

FROM THE AUTHOR'S SUMMARY.

MULTIPLE HEMORRHAGIC HEPATOMA (L'ESPERANCE). THOMAS K. RATHMELL and M. PAUL MAINS, Pediatrics **3**:508 (April) 1949.

A 5 month old white female infant presented a tumor in the right upper quadrant of the abdomen. The results of physical examination were otherwise normal, and laboratory studies provided no additional information. The clinical findings suggested the presence of a neuroblastoma, embryoma or a primary tumor of the liver. Roentgenographic studies excluded all possibility of any embryoma. Exploratory laparotomy was necessary for definite diagnosis, revealing a primary tumor of the liver confined to the right lobe. The infant died and postmortem examination showed there were no metastatic lesions. Histologic studies of the tumor tissue revealed that it was a multiple hemorrhagic hepatoma of L'Esperance. The case was registered with the Army Institute of Pathology. Photographs of the gross and histopathologic features are presented. Histologic areas within the tumor which appeared to be bone under routine stains were shown by modified Masson's trichrome stain to be composed of collagenous tissue. Statements to the effect that osseous tissue is present in hepatomas should be accepted with caution in view of the findings in this case. While the tumor is rare in infants, familiarity with its pathologic features should facilitate its clinical recognition. Early surgical exploration is necessary for diagnosis and institution of such therapeutic procedures as may be considered essential for recovery.

FROM THE AUTHORS' SUMMARY.

HOMOLOGOUS SERUM HEPATITIS IN INFANTS AND CHILDREN. RALPH E. MOLOSHOK, SAMUEL KARELITZ and LOTTE STRAUSS, Pediatrics **3**:651 (May) 1949.

Eight cases of homologous serum hepatitis are reported in 7 infants under 1 year of age and in a child 2½ years old. Five of these children died of acute hepatic

degeneration. Suggestive evidence is presented for the implication of icterogenic plasma in 5 of the patients. The clinical, laboratory and postmortem findings of serum hepatitis are described in detail. Preventive measures are reviewed and summarized.

FROM THE AUTHORS' SUMMARY.

ESTIMATION OF ALTERATIONS OF SERUM GAMMA GLOBULIN BY A TURBIDIMETRIC TECHNIQUE. Henry G. Kunkel, Proc. Soc. Exper. Biol. & Med. **66**:217 (Oct.) 1947.

Dilution of serum with solutions of salts of heavy metals was found to precipitate various protein fractions according to the concentration of the metal used. Electrophoretic analyses showed that at the lower concentration the precipitate consisted almost entirely of gamma globulin. The precipitated globulin could be accurately determined by turbidity measurements because the protein precipitated as a diffuse finely particulate suspension. Zinc, mercury, lead and cadmium salts were found to produce an effect similar to that of copper sulfate. The best differentiation between the two types of serum, that is, serum of normal persons and that of patients with hepatitis, occurred at p_H 6.5 to 7.5 in the presence of as low an ionic strength as it is practical to use. For routine use the solution eventually employed contained 24 mg. of white vitriol ($ZnSO_4.7H_2O$), 280 mg. of barbituric acid and 210 mg. of sodium barbiturate per liter. The p_H was 7.5. The procedure used was to measure 1 volume of serum (0.05 cc.) into 60 volumes of either the copper sulfate or the zinc sulfate reagent; this was allowed to stand for thirty minutes and then shaken, and the turbidity was read in the spectrophotometer at 650 millimicrons. Approximately 1,000 determinations with the copper and zinc turbidity reactions have been carried out on various serums. The normal range was found to lie between 2 and 8 units. Certain serums with globulin levels above 6 Gm. per hundred cubic centimeters have shown values as high as 80 units. In these serums more than half of the protein was precipitated. A close relationship between the turbidity in units and the globulin level of the serum was found. Patients with multiple myeloma showed turbidity in proportion to the increase in gamma globulin. All 41 patients with cirrhosis of the liver were tested and observed to demonstrate a positive reaction. The test was of particular value when applied serially throughout the course of an acute illness. The authors reported that another application with the zinc turbidity test was the study of gamma globulin in association with the development of antibodies following scarlet fever and rheumatic fever. Increased turbidity was noted to parallel closely the rise in antistreptolysin and antistreptokinase titers. The estimation of the increase in gamma globulin really measures the total globulin elevation in pathologic serums because hyperglobulinemia is almost always due to the alteration in the gamma globulin fraction of the serum. This technic was observed to be of particular value in the detection of persistent hepatic damage following infectious hepatitis.

HANSEN, Galveston, Texas.

COMPLETE DUPLICATION OF THE LARGE BOWEL TREATED BY SUBTOTAL COLECTOMY. CHARLES A. ALLARD, DUDLEY E. ROSS and J. F. HOPKIRK, Canad. M. A. J. **60**:165 (Feb.) 1949.

Complete duplication of the large bowel, with involvement of the terminal portion of the ileum and a urethral fistula, is reported. The condition was treated by subtotal colectomy, with preservation of the rectum.

McGUIGAN, Evanston, Ill.

PAROTITIS IN THE CONJUNCTIVO-GLANDULAR SYNDROME OF PARINAUD. H. KOUMROUYAN, Schweiz. med. Wchnschr. **79**:1045 (Nov.) 1949.

Two cases of the unilateral conjunctivoglandular syndrome of Parinaud are described. Both patients were 11 year old girls, and both had parotitis.

AMBERG, Rochester, Minn.

Nervous Diseases

THE TREATMENT OF PNEUMOCOCCIC MENINGITIS WITH MASSIVE DOSES OF SYSTEMIC PENICILLIN. HARRY F. DOWLING, LEWIS K. SWEET, JAY A. ROBINSON, WILLIAM W. ZELLERS and HAROLD L. HIRSH, Am. J. M. Sc. **217**:149 (Feb.) 1949.

Twenty-one patients with pneumococcic meningitis were given 1,000,000 units of penicillin intramuscularly every two hours. Three of them received a single intrathecal injection of penicillin; the others were given no intrathecal therapy. Thirteen patients received sulfonamides in addition. There were 8 deaths, a case fatality rate of 38 per cent, compared with 41 deaths (62 per cent) among the 66 patients previously treated with smaller doses of penicillin systemically plus repeated intrathecal injections of penicillin.

In the patients who recovered, the temperature dropped more rapidly among those who received massive systemic doses than among those who were given repeated intrathecal injections. Likewise the duration of pleocytosis was shorter in the former group.

Since the results of massive systemic penicillin therapy in pneumococcic meningitis are at least as good as and apparently better than those obtained with the conventional systemic doses of penicillin plus multiple intrathecal doses, it is recommended that all patients with pneumococcic meningitis be given 1,000,000 units of penicillin intramuscularly at two hour intervals. Patients in coma or dying when treatment is begun may be given a single initial intrathecal dose of penicillin in addition. Administration of sulfonamides does not appear to be necessary when these doses are used.

HENSKE, Omaha.

DISTENTION OF THE SUBARACHNOID SPACE WITH CEREBROSPINAL FLUID IN INFANTS: ENLARGEMENT OF THE HEAD AND SPASTICITY: SURGICAL CORRECTION. CHARLES BAGLEY JR., RAYMOND K. THOMPSON and R. M. N. CROSBY, Ann. Surg. **129**:662 (May) 1949.

The purpose of this paper is to segregate, from a large group of infants with increased intracranial pressure due to excess of cerebrospinal fluid, a specific group in which the clinical picture is sufficiently uniform to constitute a clinical entity. The salient features are: (1) increased intracranial pressure, (2) irritative signs and (3) distention of a subarachnoid space with cerebrospinal fluid. This condition is produced by bloody cerebrospinal fluid.

Drainage of the subarachnoid space was the therapy used by the authors. The simplest type of drainage is obtained through repeated lumbar punctures. The best guide of therapy is the tension of the fontanel. If lumbar punctures do not keep the tension down, craniotomy with free and maintained drainage of fluid from the subarachnoid space is indicated.

BANTIN, Omaha.

A Case of Meningitis Due to Pseudomonas Aeruginosa (Bacillus Pyocyaneus) and Neisseria Flavescens with Recovery. Ryle A. Radke and Guy C. Cunningham, J. Pediat. **35**:99 (July) 1949.

Radke and Cunningham report a case of primary meningitis in a 3 year old boy. The organisms were Pseudomonas aeruginosa and Neisseria flavescens. He was treated with streptomycin and recovered with residual symptoms.

Macdonald, Pittsburgh.

Acute Focal Edema of the Brain in Children with Head Injuries. Wilfred Pickles, New England J. Med. **240**:92 (Jan. 20) 1949.

By means of 8 cases in his own experience and the observations of several authorities on head injuries, the author lends his support to the arguments in favor of the existence of a post-traumatic state which may resemble extradural bleeding. This he terms acute focal edema of the brain with concomitant capillary anemia. Several typical case histories are given of children who appeared initially to have serious intracranial bleeding, which was not confirmed by the rapid clinical recovery or the visible findings at operation. The early clinical syndrome may be indistinguishable from that encountered in intracranial hemorrhage, that is, unconsciousness, vomiting, shock, convulsions, paresis and/or paralysis. Complete recovery is common.

Wheelock, Denver.

B. Mucosus Capsulatus (Friedländer) Meningitis: Recovery of a Three-Week-Old Infant Treated with Sulfadiazine and Streptomycin. W. A. Daniel Jr., Pediatrics **3**:3 (Jan.) 1949.

A case is reported of a 3-week-old infant with meningitis who showed Bacillus mucosus capsulatus (Klebsiella pneumoniae) on culture of the spinal fluid. Recovery followed treatment with sulfadiazine and streptomycin.

Perhaps the greatest difficulty encountered in B. mucosus capsulatus meningitis is in diagnosis. The adult patient usually has a primary source of infection, but this is the exception in the infant. As a rule, there are no symptoms indicating involvement of the central nervous system in spite of the severe illness of the patient. The results of approximately one fourth of all initial examinations of the spinal fluid in reported cases have been termed normal. Early examination of spinal fluid is imperative, because it may be impossible to obtain spinal fluid after the infant has been ill several days. The treatment consists of adequate administration of sulfadiazine and streptomycin. Whether streptomycin should be given intrathecally is an unsolved problem. But, until there is more evidence against it, it seems wise to introduce streptomycin into the spinal canal. Early diagnosis and adequate treatment with both sulfadiazine and streptomycin will be followed by recovery.

From the Author's Summary.

Infantile Cerebral Palsy Cases with Severe Mental Deficiency: Relationship of Etiology to Type of Neurologic Syndrome. Herman Yannet, Pediatrics **3**:820 (June) 1949.

This is a report of a study on 157 cases of infantile cerebral palsy planned to demonstrate the correlation of etiologic diagnosis with neurologic residuals. The average mental level of the group as a whole is represented by an intelligence quotient of 25, indicating the restricted distribution of the clinical material. Birth trauma or postnatal infections of the central nervous system were observed to be

of etiologic importance in almost one third of the cases with asymmetric spastic involvement. On the other hand, these causative factors were not implicated in any of the hypotonic or ataxic group, or in those cases of cerebral palsy with symmetric involvement.

FROM THE AUTHOR'S SUMMARY.

BRAIN TUMORS IN CHILDREN. HADDOW M. KEITH, WINCHELL McK. CRAIG and JAMES W. KERNOHAN, Pediatrics **3**:839 (June) 1949.

A review of 427 brain tumors in children proved by histologic study is presented. Twenty-four per cent of all tumors were astrocytomas, 20 per cent medulloblastomas and 11 per cent ependymomas. Gliomas constituted 84 per cent of all the tumors in the series. Tumors were observed in 6 infants 1 year old or younger, 2 being in infants 2 months old. Medulloblastomas and ependymomas were distinctly commoner in children under 6 years of age. Sixty-six of all tumors were infratentorial.

Under present conditions at the Mayo Clinic, Rochester, Minn., 54 per cent of all children who undergo operation for tumor of the brain survive for six months or more. Of 356 patients observed for five years or more after operation, 13.3 per cent survived for at least five years. The longest survival period was twenty years after the removal of an astrocytoma and such a patient still has a life expectancy.

FROM THE AUTHORS' SUMMARY.

AN EVALUATION OF ELECTROENCEPHALOGRAPHY IN THE DIAGNOSIS OF BRAIN TUMORS OF CHILDREN. JOHN F. DRUMHELLER, HADDOW M. KEITH and REGINALD G. BICKFORD, Pediatrics **4**:114 (July) 1949.

A study was made of the electroencephalograms of 50 children who had proved neoplasms of the brain. In 9 of 12 children who had tumors of the cerebral cortex, the localization afforded by the electroencephalogram was correct. In 8 children who had supratentorial tumors of or near the brain stem, no localizing or consistent eletroencephalographic pattern was observed. In 21 of 30 children who had tumors of the posterior fossa, a bilateral abnormality was observed in the electroencephalograms recorded from the occipital region or the occipital and contiguous regions.

It is acknowledged that the abnormality observed in this last group also is seen occasionally in conditions other than brain tumors of the posterior fossa. These conditions usually can be excluded by the use of the history and other laboratory aids. Electroencephalography in the study of brain tumors in children should be considered not as an infallible test but rather as a diagnostic aid to be used and evaluated with the help of a clinical history and other diagnostic and laboratory aids.

FROM THE AUTHORS' SUMMARY.

BIRTH INJURY, FOCAL EPILEPSY AND CORTICAL EXCISION: CASE REPORT. WILDER PENFIELD and SAMUEL LIVINGSTON, Pediatrics **4**:157 (Aug.) 1949.

This 8 year old boy had a cerebral hemorrhage at birth. In spite of this, however, he held up his head at 3 weeks and sat alone at 4 months of age. Mental development seemed to be normal until he reached 6 months of age. Recurring cerebral seizures began at 5 months and soon thereafter there was notable deterioration. At 12 months, when he was operated on, he could not hold up his head and was completely apathetic. Thereafter, seizures stopped and improvement, both mental and physical, followed. The patient is now 8 years of age. He has been entirely free of convulsions since about 15 months of age (three months

after the operation). He is in the second grade. He has a chronologic age of 8 years 4 months, a mental age of 6 years 2 months and an intelligence quotient of 74 per cent.

FROM THE AUTHORS' SUMMARY.

SALMONELLA NEWPORT MENINGITIS. L. N. PEARLMAN and A. S. P. GORDON, Canad. M. A. J. **60**:483 (May) 1949.

A rare case of Salmonella newport meningitis is presented. The patient, 3 months old, was apparently perfectly normal six months later. Treatment consisted of administration of streptomycin and sulfadiazine.

McGUIGAN, Evanston, Ill.

THROMBOSIS OF SUPERIOR LONGITUDINAL SINUS IN AN INFANT TREATED WITH HEPARIN IN AN INTRAVENOUS DRIP. S. VAN CREVALD, J. I. DE BRUYNE and M. G. STRONK, Nederl. tijdschr. v. Geneesk. **93**:1144 (April 9) 1949.

A baby with a congenital heart failure combined with cyanosis showed, when 3 months of age, symptoms which had to be regarded as the consequence of a thrombosis of the superior longitudinal sinus. These symptoms disappeared completely after intravenous administration of fluid and heparin. Two months later the baby died from bronchopneumonia after a short illness and without showing neurologic symptoms. At the autopsy a transposition of the large vessels was observed with a small defect in the interauricular septum. A canalized thrombosis of the superior longitudinal sinus was present. In the region of the large fontanel this sinus showed a spongy brownish tissue in which at microscopic examination bands of connective tissue with blood pigments were seen, while locally active organization was still present with many cells having a round nucleus and iron pigment. Along the longitudinal sinus the pia mater was brownish and thickened. In the brain, especially in the left parietal region in the cortical and subcortical zone, a distinct focus of softening was present.

VAN CREVELD, Amsterdam, Netherlands.

Psychology and Psychiatry

THE PSYCHIATRIST'S ROLE AT THE ILLINOIS CHILDREN'S HOSPITAL SCHOOL. HAROLD A. GREENBURG, Illinois M. J. **95**:285 (May) 1949.

The Illinois Hospital School was designed to provide restorative treatment and educational facilities on a twenty-four hour residential basis for selected children on a long term plan. It was set up for children whose educational and physical needs could not be met through available facilities. In 1947 Greenburg was appointed psychiatric consultant to the school.

The author has found that the psychiatrist is able to bring to a hospital school the technics used in the diagnosis and treatment of psychologically disturbed children, technics which include a full understanding of total staff responsibility. These are methods which are inherent in modern residential schools for the treatment of such children and have been generally followed by the staff of the Illinois Hospital School. By staff responsibility is meant that the staff is considered as a total working team, with each member as important as any other in his relationship to the children. Every employee is potentially a parent substitute to the child, and it is for this reason that the psychiatrist emphasizes to the staff the necessity for total staff integration and responsibility. The psychiatrist's function in such a school consists in the main in attempting to understand the children's emotional problems and the interrelationships of children and staff.

BARBOUR, Peoria, Ill.

CHRONIC RESISTANCE TO SLEEP IN INFANCY. BENJAMIN SPOCK, Pediatrics **4**:89 (July) 1949.

Chronic resistance to sleep in infancy is an increasingly frequent behavior problem which seems related to the trend toward self regulation and to confusion in the application of this philosophy. A typically modern problem is that of the uncertain, overconscientious mother, a disciple of the self-expressionist philosophy, who permits her baby to learn to resist sleep or to wake during the night and cry until picked up. Such a mother is advised to lay the infant down with affectionate but firm words and manner and leave the room. Usually three nights' treatment is sufficient to cure the sleep problem. The policy of letting the baby "cry it out" is recommended only for chronic resistance to sleep in the infant up to the age of 1 or 1½ years. It is not for the wakeful child who is sick or uncomfortable or who suffers from an acute anxiety state.

FROM THE AUTHOR'S SUMMARY.

SLEEP DISTURBANCES IN CHILDREN. C. KOHLER, Pédiatrie **36**:215 (May-June) 1947.

Sleep may be disturbed in its duration—hypersomnia or insomnia—or in its quality on a somatic or psychic basis. In insomnia there may be failure of the mental or muscular processes to rest or exaggeration of these processes. Insomnia may be partial or total and may consist in a failure of the child to fall asleep or in interrupted sleep. Among the organic causes of insomnia the author mentions intoxications and local and general infections. In infants congenital syphilis produces night cries; stimulants taken by the wetnurse will cause sleeplessness in the infant; tooth eruption, spasmophilia, faulty adjustment of conditioned reflexes and habits are other causes. In later childhood psychosomatic disturbances, such as fever, acute and chronic infections, digestive disturbances, neurologic disturbances, acrodynia, tuberculous meningitis, cerebral tumors, encephalitis and dementia precox, are more important. Neuroses, such as anxiety, are more frequent causes of insomnia; neurotic constitution and psychomotor instability are predisposing factors.

Hypersomnias are less frequent and may be caused by external or internal states of toxicosis, such as carbon monoxide intoxication or acidosis, azotemia, endocrine imbalance (as myxedema) and, the best example, epidemic encephalitis. Among the rarer causes of hypersomnia are meningitis, the preparalytic stage of poliomyelitis, brain tumors and hydrocephalus. Psychologic influences may be active and probably explainable by the attempt to escape unpleasant situations by sleep. Paroxysms of hypersomnia may be produced by narcolepsy and cataplexy.

Parasomnias, according to Kohler, are disturbances which occur during the sleep, such as convulsions, which occur because of the relaxation of the inhibitory influences of the cortex. Tics and rhythmic motions are also considered as parasomnias. Enuresis, nightmares, pavor nocturnus (night terror) and somnambulism are discussed in some detail as to their possible origin, most likely on a psychoneurotic basis. The value of psychotherapy in such cases is particularly stressed. Other disturbances of sleep (delirium, etc.) are on a basis of real mental disease rather than neurotic disturbances.

For the prevention of the disturbances, Kohler recommends strict regulation of meals and definite forbidding of pacifier and rocking, as well as proper general hygienic measures. For treatment—aside from etiologic treatment, which is not discussed—one may employ hydrotherapy, electrotherapy, hypnotics and sedatives, stimulants, such as ephedrine and, finally, psychotherapy and psychoanalysis.

GLASER, Chicago.

INCIDENCE OF NERVOUS DISORDERS IN THE FIRST YEAR OF LIFE. BERHARD BESKOW, Svenska läk.-tidning. **44**:2341 (Dec. 12) 1947.

One thousand one hundred and twenty-seven small children under 3 years of age belonging to Infant Welfare Centers in Malmö, Sweden, were supervised during their first year of life, with special attention to the incidence of nervous diseases and symptoms. Of the children, 24.9 per cent were quite normal, 32.5 per cent showed nervous symptoms during the entire observation time and 42.5 per cent displayed occasional nervous symptoms. Infants with a low weight at birth showed nervous symptoms more frequently than did infants with a mean or high weight at birth. Infants who had nervous disorders during the entire observation time showed their first symptoms in the first month of life in 87.8 per cent (boys) and in 93.1 per cent (girls). There was no preponderance of first-born infants in this group, as compared with the group of infants with no nervous symptoms, which indicated that the nervousness of the first-born child depends on external causes.

WALLGREN, Stockholm, Sweden.

Diseases of the Genitourinary Tract

OVARIAN TUMORS IN CHILDHOOD. HAROLD W. DARGEON, Pediatrics **3**:773 (June) 1949.

Data on 14 cases of ovarian tumors occurring in children are discussed in this presentation. Ovarian neoplasm is uncommon during childhood. It should be considered, however, in the differential diagnosis of several conditions observed not infrequently by the clinician in girls from infancy through adolescence. These conditions are lower abdominal pain of acute, subacute or chronic nature, abdominal or pelvic masses, precocious puberty and vaginal bleeding. The treatment is surgical. The prognosis in patients with the malignant varieties is usually serious, but there are exceptions to this generalization. The prognosis in those with the benign types is good.

FROM THE AUTHOR'S SUMMARY.

PORPHYRINURIA: REPORT OF AN UNUSUAL CASE. NORMAN C. WOODY, Pediatrics **4**:47 (July) 1949.

An infant born of a mother with acute porphyria excreted excessive amounts of uroporphyrin and coproporphyrin in the urine during the first few weeks following birth. In the course of the next several months the infant was entirely free from unusual signs or symptoms, except that her stature at 11 months was short. No similar case has previously been recorded. The term "passive porphyrinuria" is suggested to describe this condition.

While an excess of porphyrins in the fetal environment may have resulted in stunting of growth, other evidences in this patient offer support to the belief that the pathologic lesions of porphyria result from the metabolic error and not from the presence of these pigments per se.

FROM THE AUTHOR'S SUMMARY.

BLOOD CONCENTRATION AND URINARY ELIMINATION OF SULFONAMIDES IN ACUTE RENAL DISORDERS. R. PACHIOLI, Clin. pediat. **30**:305 (May) 1948.

The blood concentration and urinary elimination were determined following the administration of 0.2 Gm. of sulfathiazole for one day in four doses to healthy children and to children with mild and moderately severe glomerulonephritis. Whereas in the normal children all the drug was excreted in thirty hours, in the

nephritic children excretion was not complete until forty-two to one hundred and two hours after the last dose was given.

In view of the slowness of excretion, due to lowered renal function, sulfonamide drugs should not be given to nephritic children without careful control studies of the blood concentration of the drug.

HIGGINS, Boston.

ATYPICAL HYPERNEPHROID TUMOR IN A BOY FOUR MONTHS OLD. L. LANDUCCI, Lattante **19**:336 (June) 1948.

An infant 4 months of age had a rapidly growing malignant tumor of the abdomen, which was tentatively classified as an atypical hypernephroid tumor of Lubarsch's second type.

HIGGINS, Boston.

INFREQUENT MENINGEAL AND ENCEPHALITIC SYNDROMES IN CHILDREN WITH UREMIA.' ANGIOLA CANUBI, Pediatria **56**:266 (April) 1948.

Three cases of acute hemorrhagic nephritis with symptoms of convulsions, psychoses and meningeal irritation are reported. The possible bases of these symptoms, cerebral edema, vasospasm and toxemia, are discussed.

HIGGINS, Boston.

PYELOCYSTITIS IN A FIVE YEAR OLD GIRL CURED WITH STREPTOMYCIN. A. CARNEVALE, Pediatria **56**:308 (April) 1948.

This child had a pyelocystitis due to a colon bacillus, and had not been benefited by mandelic acid or sulfathiazole therapy. Administration of streptomycin in doses of 0.2 Gm. every four hours until a total of 7 Gm. had been given promptly relieved the condition.

HIGGINS, Boston.

SIMPLE TREATMENT FOR NOCTURNAL ENURESIS. K. LENGGENHAGER, Schweiz. med. Wchnschr. **78**:68 (Jan. 24) 1948.

The author rejects the old Krasnagorski treatment of administering a large quantity of salt at bedtime. This author directs the patient to set an alarm clock for some time during the night. If the patient wets the bed before the alarm sounds, it is set for several hours earlier the next night. The author maintains that this simple method establishes a good habit of emptying the bladder, and he states that it is astonishing how well this plan works and how much it improves the inferiority complex of affected children.

ABT and ABT, Chicago.

THE DIFFERENCE CURVE: A SIMPLE AID FOR CONTINUOUS DETERMINATION OF RENAL FUNCTION AT THE BEDSIDE. K. WALTHER, Med. Klin. **44**:150 (Feb. 4) 1949.

The specific gravity of each specimen of urine is taken and the difference between the lowest and the highest specific gravity in twenty-four hours is registered on the temperature chart, allowing a quick orientation of renal function. In an illustrative curve for a case of contracted kidney it is a little disconcerting to find values below zero registered.

AMBERG, Rochester, Minn.

NEW METHODS OF TREATMENT OF ACUTE TEMPORARY RENAL DEFICIENCY. CURT MOELLER, Med. Klin. **44**:397 (April 1) 1949.

The author discusses continuous peritoneal drainage and the "artificial kidney." He reports a case in which continuous drainage by way of the bladder with

isotonic sodium chloride solution was carried out and calculates that 10 Gm. of urea over the average urinary excretion of urea could be removed in this manner.

AMBERG, Rochester, Minn.

TREATMENT OF SEVERE OLIGURIA AND ANURIA WITH ROENTGEN RAYS. ROBERT HEINTZ, Med. Klin. **44**:496 (April 22) 1949.

Three patients, 1 of whom was a 5 year old girl with postscarlatinal nephritis accompanied with severe oliguria, responded to roentgen therapy with diuresis.

AMBERG, Rochester, Minn.

Diseases of the Ductless Glands; Endocrinology

TREATMENT OF HYPERTHYROIDISM IN CHILDREN. JOHN H. LYONS, Ann. Surg. **129**:631 (May) 1949.

Hyperthyroidism is a rare disease in children. It has, however, been diagnosed in infancy. The disease is especially rare in male children. In the past thirteen years, in 78,659 admissions only 8 children with the disease have entered the Children's Hospital, Washington, D. C. No more is known about the origin of hyperthyroidism in children than in adults. Certain predisposing or exciting factors are recognized. Heredity may play an important part. In some patients hyperthyroidism seems to follow an infectious disease or psychic trauma.

Because of the failure of thiouracil and related drugs to live up to the expectations of pediatricians, the uncertain results of roentgen therapy and the dangers associated with the use of radioactive iodine, subtotal thyroidectomy remains the best treatment for hyperthyroidism in children.

Careful preparation must precede operation. It is the author's firm conviction that iodine is the drug of choice in preparing children with hyperthyroidism for operation and that propylthiouracil should be used only for those patients in whom iodine fails to reduce the basal metabolic rate and allay the symptoms so that a single stage thyroidectomy can be carried out safely.

BANTIN, Omaha.

HYPERFUNCTIONING TUMORS OF THE ADRENAL CORTEX WITH REPORT OF EIGHT CASES. WALTMAN WALTERS and RANDALL G. SPRAGUE, Ann. Surg. **129**:677 (May) 1949.

The authors present a group of 8 patients with proved tumors of the adrenal cortex. Three were in children. The clinical pictures associated with hyperfunction of the adrenal cortex are extremely protean in nature and presumably depend on the type and quantity of steroid hormones produced, the age and sex of the patient and perhaps other factors. For patients presenting clinical syndromes known to be associated with hyperfunction of the adrenal cortex, the problem of differentiating between tumor and hyperplasia has been simplified by methods of urinary assay.

Results following removal of hyperfunctioning tumors of the adrenal cortex are good in general and are excellent if the lesion is benign. Results following operation in patients with adrenal hyperplasia are less satisfactory.

BANTIN, Omaha.

OCULAR FINDINGS IN ONE HUNDRED AND TWENTY-EIGHT JUVENILE DIABETICS. I. GIVNER and C. LODYJENSKY, New York State J. Med. **47**:1371 (June 15) 1947.

In routine funduscopic examination of 128 diabetic children, Givner and Lodyjensky found 3 who had retinal hemorrhages and 1 who had diabetic cataract. Since none of the patients had complaints referable to vision, and since the importance of retinal hemorrhages in a better evaluation of the case has been emphasized, it would seem good practice to study every diabetic patient under mydriasis. Special emphasis should be put on pinpoint hemorrhages and aneurysmal capillary dilatations, as they can be easily overlooked.

J. A. M. A. (ZENTMAYER).

LAURENCE-MOON-BIEDL-BARDET-SYNDROME AFTER GRIP OF THE MOTHER DURING PREGNANCY. K. W. NIEDERER, Schweiz. med. Wchnschr. **79**:1061 (Nov. 5) 1949.

A man 30 years of age, whose mother had grip in the third month of pregnancy, was seen with a typical Laurence-Moon-Biedl-Bardet syndrome.

AMBERG, Rochester, Minn.

CUSHING'S SYNDROME IN A TWENTY MONTH OLD GIRL. K. WEISSE, Ztschr. f. Kinderh. **65**:9, 1947.

The author discusses Cushing's disease as caused by a basophilic adenoma of the pituitary gland, producing adiposity, osteoporosis, hypertonicity, hypertrichosis, sexual disturbances, metabolic changes and purplish striae. Similar symptoms may be produced by pathologic changes in the adrenal cortex or by a tumor of other organs and are referred to by this author as Cushing's syndrome.

The case of a 20 month old girl is presented. This patient showed adiposity of the whole body, especially the face, hypertrichosis, lowering of the voice, easy fatigability, personality changes, bluish red discoloration of the skin and venous ectasia over the entire body. The fundi, heart and visual fields and the roentgenograms of the skull were normal. The blood pressure was 170 systolic and 130 diastolic and remained elevated for several weeks. The genitalia were hairy and the clitoris and labia were hypertrophied, considering the age of the patient. No ovarian, renal or adrenal masses were felt. Polyphagia was prominent. Blood cholesterol was between 167 and 183 mg. per hundred cubic centimeters, which in the author's opinion was slightly elevated. The fasting blood sugar, between 80 and 90 mg. per hundred cubic centimeters, was also considered slightly elevated for a patient of this age. Sugar tolerance curves deviated from the normal. The intravenous pyelogram and the roentgenographic study of the duodenum showed nothing abnormal. 17-ketosteroids were determined by the biologic assay method and colorimetrically; results obtained by the latter method were three times as high as those obtained by the biologic method. Laparotomy revealed a tumor the size of a chicken egg in the left adrenal gland which was removed. However, despite sodium chloride infusions and administration of vitamin C and cortical hormone (10 mg. intravenously daily, later believed to have been too small a dose), the child died on the third postoperative day, after the blood pressure had dropped to 150 systolic and 95 diastolic on the second day. The specimen showed an immature adrenocortical adenoma and increase in the size of some islands of Langerhans. It is believed that stimulation of the adrenal cortex by increased secretion of corticotropic hormone and, conversely, disturbance of the hypophysis

by increased cortical secretion account for the similarity in the clinical and laboratory findings in Cushing's syndrome and in true Cushing's disease.

GLASER, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Nodes

ACUTE MESENTERIC LYMPHADENITIS. R. W. POSTLETHWAIT and FRANK H. CAMPBELL, Arch. Surg. **59**:92 (July) 1949.

The authors analyzed the symptoms of 268 patients treated surgically for abdominal pain and tenderness in whom a grossly normal appendix was found but enlargement of mesenteric lymph nodes was encountered. A diagnosis of nonspecific mesenteric lymphadenitis was made for these patients. A study of 1,604 patients with the symptoms and signs of an acute condition in the abdomen which led to treatment by appendectomy supplied the 268 cases discussed.

The authors summarize their report by stating that nonspecific mesenteric lymphadenitis is a symptom complex, characterized by abdominal pain and tenderness. Many of the patients have a history of prior attacks of pain and about one-half the patients have an infection of the upper respiratory tract. The pain frequently comes in paroxysms, with intervals of complete relief. Tenderness is usually present in the right lower quadrant, but signs of peritoneal irritation occur in only about one third of the cases. Operation, with removal of the appendix, is strongly advised, as an accurate differential diagnosis between mesenteric lymphadenitis and acute appendicitis cannot be made.

KAISER, Rochester, N. Y.

A CASE OF AMYOTONIA CONGENITA ASSOCIATED WITH OCCLUSION OF THE SAGITTAL SINUS AND BILATERAL SUBDURAL HYGROMA. MICHAEL SCOTT, J. Pediat. **34**:181 (Feb.) 1949.

The cause of the occlusion of the sinus in this case is not known. Scott theorizes as to the pathogenesis of the condition resulting from the occlusion in this case. The obstruction blocked the flow of subarachnoid fluid draining into the sinus via the arachnoid villi. The hygroma was the result. The occlusion also blocked the venous drainage from the paracentral lobule. This suppressed the development of the lobule, which is parasagittal and innervates the lower extremities. The retarded development or function of the motor cortex of the paracentral lobule retarded, in turn, the development or function of the anterior horn cells and, finally, caused abnormal development of the muscles of the extremities. This may be one cause of the syndrome of amyotonia congenita.

MACDONALD, Pittsburgh.

CRUSH SYNDROME: POST-TRAUMATIC ANURIA; OBSERVATION ON GENESIS AND TREATMENT. A. C. CORCORAN and IRVINE H. PAGE, J. A. M. A. **134**:436 (May 31) 1947.

Post-traumatic anuria (crush syndrome) is a special instance of a group of related states of renal injury. These fall in two groups, namely, those in which the principal lesion is obstruction of the renal tubules by pigmented (myoglobin, hemoglobin) casts and those in which the injury lies principally in necrosis of the epithelium of the distal convoluted tubules. The underlying mechanism in all of these, and especially in those associated with trauma to muscle tissue, is vasoconstrictive renal ischemia. This ischemia results in oliguria, which, associated with aciduria, predisposes to precipitation of pigment casts. Tubular injury due to ischemia and a hypothetic toxic agent may contribute to the renal damage.

In the presence of such renal ischemia, myoglobinuria and hemoglobinuria, which cause little injury under normal conditions, result in severe renal injury. Attention is directed to the danger of transfusing blood which has been inadequately refrigerated.

Treatment of crush syndrome and the related states is preventive and consists in the prevention of renal vasoconstrictive ischemia by prompt treatment of shock (transfusion of blood or plasma), the lessening of absorption from areas of injury by pressure bandaging and the establishment of a rapid rate of urinary flow by the administration of a diuretic. Urinary alkalization is advisable, but vigorous treatment with alkalis is dangerous.

It was shown by direct means that stimulation of renal vasomotor nerves results in a change in the pattern of renal blood flow by which the cortex, which normally receives most of the renal blood flow, becomes ischemic, the stream being diverted into the medulla. It is suggested that this vasomotor mechanism may underlie the renal cortical ischemic injury of crush syndrome and allied states and that the prevention of renal injury due to this mechanism may be accomplished by procedures which block renal vasomotor pathways (splanchnic block; high spinal or caudal anesthesia).

The authors' failure to demonstrate an important vasomotor participation in experimental crush syndrome may have resulted from their observations having been made in anesthetized animals. In these, by indirect means, they showed previously that some redistribution of cortical blood flow occurred in the renal ischemia due to bleeding or tourniquet shock. This renal ischemia was only slightly affected by renal denervation. It thus seems likely that the humoral vasoconstrictors of severe shock act on the renal circulation in a manner similar to that of intense vasomotor stimulation, i. e., by causing constriction of the cortical interlobular arteries, with cortical ischemia and diversion of blood into the medulla. Clinically, the use of procedures which block renal nerves should, therefore, be explored in the early treatment of crush syndrome and related states. The nature of the renal lesions does not suggest that such treatment will be of avail once renal ischemic damage and pigmentary occlusive and toxic injury are well established.

FROM THE AUTHORS' SUMMARY.

Diseases of the Eye

OPERATION FOR PERSISTENT PUPILLARY MEMBRANE: REPORT OF A CASE. Z. BÁTHORI, Brit. J. Ophth. **32**:505 (Aug.) 1948.

A woman aged 30 had always had poor vision. Corrected vision equaled 5/50 in the right eye and 5/12 in the left eye. In the right eye the pupillary area was occupied by a mass of brownish tissue, identical in color with the iris and slightly prominent. The slit lamp beam showed a dense central part 1.5 mm. in diameter, from which originated a mesh of threads of varying thickness passing radially toward the crypts of the iris. The pupillary margin could be seen through the mesh, and the pupil was active. The lens appeared clear. The left eye showed a similar but less distinct picture. Here, the central dense mass was only 0.5 mm. in diameter. The lens, media and fundus showed no abnormal changes. The right eye was operated on by Imre. After an incision with the keratome, the filaments were pulled into the wound, one by one, with a small iris hook and severed with de Wecker scissors, and eventually the whole pupillary membrane was removed. After operation, the entire area of the pupil was clear, and vision had improved to 5/8.

W. ZENTMAYER [ARCH. OPHTH.].

AN UNUSUAL CONGENITAL DEFECT. A. H. BRIGGS and D. W. MCLEAN, Brit. J. Ophth. **33**:381 (June) 1949.

The authors described a congenital anomaly in a girl 14 days old. The pregnancy and labor were apparently normal. Examination of the child at the age of 6 years revealed a large coloboma of the iris on the nasal side which was completely filled by a rounded pink mass with fine vessels running over its surface. Over the base of the tumor the cornea showed two islands of grayish opacity, resembling arcus senilis. Thin strands of pupillary membrane were present. Refraction revealed a high, irregular astigmatism. The disk showed situs inversus. There was complete absence of inflammatory reaction.

CONGENITAL ECTOPIA OF THE LENS WITH SPHEROPHAKIA AND SHORT STATURE, ACCOMPANIED WITH PARALYSIS OF GAZE (MARCHESANI'S SYNDROME). W. STADLIN and D. KLEIN, Ann. d'ocul. **181**:692 (Nov.) 1948.

Ectopia lentis is frequently associated with other congenital defects, as in Marfan's syndrome. Arachnodactyly is characterized by increase in length, laxness of ligamentous structures and other congenital defects. Marchesani (1939) described another syndrome, characterized by brachydactyly, ectopia lentis and spherophakia. Patients with this syndrome have round heads and short, stalky limbs, and the motility of their joints is normal.

The authors describe a patient who presented the signs and symptoms of this syndrome, as well as supranuclear paralysis of gaze. The genealogy of the patient is presented. The parents were second cousins; the mother was short and stocky, and the father had very small hands and feet. It is probable that the Marfan and the Marchesani syndrome differ only in that one shows hyperplastic and the other hypoplastic disturbances in the skeletal system. Schmid has linked the two conditions under the term "dysmorpho-dystrophia mesodermalis congenita."

P. R. MCDONALD [ARCH. OPHTH.].

PRIMARY COMPLEX OF THE CONJUNCTIVA. RUBENS BELFORT MATTOS, Arq. brasil. de oftal. **11**:7, 1948.

A girl aged 4 years had had a hordeolum in the right eye for five months. The right palpebral fissure was of normal size but was slightly irregular in the upper internal portion. The upper lid showed loss of substance of about 1 mm. in the internal third to the roots of the eyelashes, with various infected glands. On the upper lid, at the internal third, was observed a perfectly outlined formation, measuring 1 by 1.5 cm., of irregular form with tissue proliferation in the form of follicles, some of which were ulcerated. A week later, after the use of sulfanilamide, material for biopsy was obtained. In the center of a section of skin there was an inflammatory nodule, the central portion of which was necrosed. Surrounding it was histiocytic reaction with Langhans giant cells. Surrounding this was lymphocytic infiltration. A diagnosis of active tuberculosis was made. General tonics and preparations of vitamins A and D and mineral salts were prescribed.

M. E. ALVARO [ARCH. OPHTH.].

STURGE-WEBER SYNDROME WITH MELANOSIS OCULI. J. ARJONA, Arch. Soc. oftal. hispano-am. **8**:1207 (Dec.) 1948.

After discussing fully the etiology and symptomatology of the Sturge-Weber syndrome, Arjona reports a case of his own which presented special characteristics. A boy aged 13 with oxycephaly and subnormal mentality presented nevus flammeus

of both sides of the face and other parts of the body, hydrophthalmos of the left eye and congenital glaucoma of the right eye, convulsions involving the right side of the body and blue scleras. The roentgenograms showed calcareous changes in the occipital lobe of the brain. The blue scleras were produced by melanosis of this coat. According to the author, this symptom has not been mentioned in connection with the syndrome before except in a case reported by Ida Mann, in which the condition occurred with nevus flammeus but without the other symptoms of the syndrome.

The bilaterality of the nevus flammeus and ocular symptoms and the occurrence of blue scleras, which the author considers a part of the syndrome, are the unusual features of the case. The article contains a bibliography and is illustrated.

H. F. Carrasquillo [Arch. Ophth.].

Neuroparalytic Familial Keratitis and Multiplex Hereditary Neurodegeneration in a Family. Michel Jequier and Arnold Verrey, Schweiz. med. Wchnschr. **80**:38 (Jan. 14) 1950.

These cases of neuroparalytic familial keratitis were seen in members of a prolific family with 387 members in the seventh generation. Consanguinity occurred frequently. Aside from other neurologic taints, 4 presented corneal and conjunctival anesthesia. These patients had ulcerations of the cornea during the first two years of life, leaving important visual difficulties.

Amberg, Rochester, Minn.

Book Reviews

Lehrbuch der allgemeinen Kinderpsychiatrie: Einschliesslich der allgemeinen Psychiatrie der Pubertät und Adoleszenz. Third edition. By M. Tramer, M.D., Ph. D. Price, 38 Swiss francs. Pp. 549. Benno Schwabe & Co., Klosterberg 27, Basel 10, Switzerland, 1949.

This book has the following chapter headings:

I. Introduction to child psychiatry.

II. Review of the psychologic approach in relation to the child, including general introduction to psychology.

III. Development, including physical development, general psychologic development and psychosexual development in childhood and puberty.

IV. Methods of examination.

V. General psychopathology.

VI. Etiology in relation to constitution and age group.

VII. Forms of general psychopathology in relation to instincts, drives, emotions, intelligence, will, character and temperament: psychopathologic types of childhood and adolescence; criminal types; general discussion on speech disturbances and complexes.

VIII. Clinical pictures of psychic disturbances in relation to infectious diseases, endocrine disturbances, avitaminoses, psychosomatic diseases, psychopathic disturbances, neuroses and psychoses.

IX. Diagnosis and prognosis.

X. Treatment: physical therapy, individual psychotherapy and group therapy.

XI. Social function of child psychiatry.

XII. Mental hygiene in child psychiatry.

XIII. Conclusion.

XIV. Twenty-seven case histories from child psychiatric practice.

An index of contents and an index of authors are also included.

The author has considered the European literature extensively and some American papers. His approach to clinical syndromes, to methods of study and to pathology is largely descriptive; also he takes cognizance of functional analytic concepts. As in all such eclectic books, this combination of descriptive and functional psychiatry leaves the reader somewhat confused. Furthermore, Dr. Tramer writes in a style that is difficult for American readers. For this reason, the book can be recommended more for purposes of orientation in European child psychiatry and psychology, of which it gives an excellent picture, and for its exhaustive bibliography, than for its practical use to American workers in the field.

Physiology in Diseases of the Heart and Lungs. By Mark D. Altschule, M.D., Price, $5. Pp. 368, with no illustrations. Harvard University Press, 44 Francis Ave., Cambridge 38, Mass., 1949.

This book fills a gap in medical literature which has been apparent for some time. Many students and physicians must find it difficult to keep abreast of progress in the physiologic aspects of cardiorespiratory diseases. The publication of this book provides an opportunity for bringing one's knowledge in this field up to date.

The text covers in the style of a critical review the more important clinical investigations in the cardiorespiratory field carried out in the last thirty-five years. The bibliography is of such scope and completeness that it could stand alone as a major contribution to the literature of cardiorespiratory disease.

The organization of the material is excellent. The chapter on "Chronic Cardiac Decompensation," comprising almost two thirds of the text, is divided into thirty-seven sections which greatly facilitate reference. The individual reader may want a more extensive treatment of some of the subjects presented, in which case the bibliography will be of great assistance. This book has been written for students, teachers and practitioners who "desire to enhance their appreciation and understanding of clinical phenomena." This group will be grateful to Dr. Altschule for his splendid work in their behalf.

Clinical Endocrinology. By Laurence C. Martin, M.D. (Camb.), F.R.C.P. (Lond.), Physician to Addenbrooke's Hospital, Cambridge, England, and Martin Hynes, M.D. (Camb.), M.R.C.P. (Lond.), Reader in Medicine in the University of Cambridge, England. Foreword by Sir Lionel Whitby, C.V.O., M.C., M.D., F.R.C.P., D.P.H., Regius Professor of Physic, University of Cambridge, England. Price, $4.50. Pp. 222, with 8 plates and 22 text figures. The Blakiston Company, 1012 Walnut St., Philadelphia 5, 1949.

This compact book was written with the purpose of providing the general practitioner and the medical student with information on the practical phases of endocrinology and of guiding them through the complexities of the subject. This it does in a most admirable way, and because it is so concise and well organized it can be recommended as a useful, simple handbook to be kept on the physician's desk.

As with all books of this type, specific statements are sometimes made about controversial points, but one has the feeling that they are set down after due deliberation with the view of avoiding confusion and making the text more readable. The pediatrician might lift an eyebrow now and then on reading such excerpts as these:

Diagnosis of cretinism may have to be made on clinical grounds and confirmed by a response to thyroid because biochemical investigations are usually impracticable in infants.

The state of the bowels is as reliable a guide to dosage as any: constipation indicates the need for more thyroid, and looseness or diarrhea for less.

One might question the wisdom of devoting one of the eight full page plates to the reproduction of a roentgenogram of an enlarged thymus, with the caption "thymic asthma."

On the whole, however, the reviewer must agree with Sir Lionel Whitby, who states in his foreword:

The very practical contribution of Dr. Martin and Dr. Hynes should be warmly welcomed as presenting a difficult subject in most readable form and in the best traditions of the Cambridge Medical School, with a logical approach to the many problems so that no dogmatic statement is made unless it is supported by physiological or pathological evidence.

Common Skin Diseases. Eighth Edition. By A. C. Roxburgh, M.D., F.R.C.P. Price, $7. Pp. 497, with 122 illustrations and 8 color plates. The Blakiston Company, 1012 Walnut St., Philadelphia 5, 1949.

From the point of view of the pediatrician or the general practitioner this work should be an extremely valuable one. Less voluminous and less comprehensive

than the standard treatises on dermatology, it still covers adequately virtually all cutaneous disorders that the nondermatologist is called on to diagnose and treat. Furthermore, its approach is completely practical, and the book can easily be followed as a guide in both diagnosis and therapy by one who has not had special training in dermatology, at the same time pointing out those instances in which specialized care is essential.

At the beginning of the book is an "Index to Preliminary Diagnosis." Once the nature of the primary lesion or lesions in a given case has been determined, reference to this index will indicate to the observer the disorders to be considered and where in the book specific information about them is to be found. The book contains many prescriptions entirely understandable to the American, though names from the "British Pharmacopoeia" are used, but English proprietary preparations are only rarely mentioned.

All in all, the book is highly recommended to the busy practicing pediatrician as an adequate, speedy and practical reference to expedite his management of the many problems referable to the skin for which he is called on to advise.

Communicable Disease Nursing. Second Edition. By Theresa I. Lynch. Price, $4.75. Pp. 776, with 135 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1949.

This text on communicable disease nursing is a fine reference work for nurses to use in review, as it covers quite thoroughly those diseases seen less frequently, as well as those seen every day. One realizes that knowledge of these diseases is necessary to the giving of intelligent nursing care; but the nurse might find the text much more helpful if it stressed the nursing procedures she could use in relieving and giving comfort to the patient. One keeps wishing for a text on communicable disease nursing that will include listings from units throughout the country which treat communicable diseases on life-saving and time-saving equipment with instructions on how the nurse uses them. This book has an excellent historical introduction, including world health plans, which should be of great interest to many.

Muscles—Testing and Function. By Henry A. Kendall and Florence R. Kendall. Price, $7.50. Pp. 278, with 192 illustrations. Baltimore: The Williams and Wilkins Company, 1949.

About fifteen years ago, I visited the authors and observed their work at the Children's Hospital School in Baltimore. I was most favorably impressed, as have been scores of other orthopedic surgeons, by the skill with which they were able to detect slight differences of muscle strength or muscle tonus.

Although the method of grading muscle power on a percentage basis requires training and judgment greater than most of us have in order to recognize a 5 or 10 per cent variation, the Kendalls definitely do have that ability and judgment. In addition to presenting in an understandable fashion the principles of manual muscle testing, they discuss and emphasize the importance of body mechanics. As an anatomic study alone, this book is well worth while.

The illustrations consist of excellent photographs complemented by line drawings. The Kendalls demonstrate how to measure body deficiencies other than mere muscle weakness.

Those who are interested in an optimum function of the spine and extremities, including muscles, bones, tendons and ligaments, will find this book most useful.

Directory of Pediatric Societies *

INTERNATIONAL

Sixth International Congress of Pediatrics

President: Prof. Guido Fanconi.
Secretary: Dr. H. Zellweger, Kinderklinik, Zurich.
American Committee:
President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: Zurich, Switzerland. Time: July 24-28, 1950.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Pan American Congress of Pediatrics

President: Dr. Felix Hurtado, Habana, Cuba.

International Union for Child Welfare

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quay Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriquez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Armando de Arruda Sampaio.
First Secretary: Dr. Luis Fontoura y Lauro Machado Oliveira, Caixa Postal 2103, São Paulo, Brazil.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

Asociación Pediatrica de Guatemala

President: Dr. Carlos Manuel Monzon, Plazuela Santuario de Guadalupe, Guadalupe.
Secretary: Dr. Maria Isabel Escobar, Casa del Niño no. 1, Guadalupe.

British Paediatric Society

President: Dr. A. G. Maitland-Jones.
Secretary: Dr. Alan Moncrieff, Institute of Child Health, Hospital for Sick Children, Great Ormond St., London W. C. 1.
Place: Windermere.

Bulgarian Pediatric Society

President: Dr. L. Ratchew, University Children's Hospital, Wassil Kolarow 46, Sofia.

Chinese Pediatric Society

President: Dr. W. S. Fu, The Shanghi Public Hospital for Children, 11 Hsiang Shan Road, Shanghai, China.
Secretary: Dr. T. F. Su, The Shanghai Public Hospital for Children, 11 Hsiang Shan Road, Shanghai, China.
Time: Concurrent with the annual conference of the Chinese Medical Association.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

CZECHOSLOVAK PEDIATRIC SOCIETY

Chairman: Prof. Dr. Jiri Brdlík, 2 Sokolská, Prague II.

DANISH PEDIATRIC SOCIETY

Chairman: Prof. Preben Plum.
Secretary: Dr. Elin Fog, Søllingsvey 17, Charlottenlund, Denmark.

GERMAN PEDIATRIC SOCIETY

President: Dr. H. Kleinschmidt.
Secretary: Dr. F. Goebel, 5 Moorenstrasse, Düsseldorf, Germany (British Zone).

HELLENIC SOCIETY OF PEDIATRICS

President: Dr. C. Saroglou, Patission St. 74, Athens, Greece.
Secretary-General: Dr. S. Charocopos, Alexandras Ave. 1, Athens, Greece.

INDIAN PEDIATRIC SOCIETY

President: Dr. K. C. Chaudhuri, Dept. of Pediatrics, Medical College, Calcutta.
Secretary: Dr. S. P. Bhattacharjee, Dept. of Pediatrics, Medical College, Calcutta.
Place: Office of the Indian Medical Association, 67 Dharamtala St., Calcutta 13. Time: Every second and fourth Wednesday of each month.

MEDICAL ASSOCIATION OF ISRAEL, NATIONAL PEDIATRIC SOCIETY

President: Prof. L. F. Meyer, 29 Idelson St., Tel-Aviv, Israel.
Secretary: Dr. W. Hirsch, Hadassah Municipal Hospital, Tel-Aviv, Israel.

NEDERLANDSCHE VEREENINGING VOOR KINDERGENEESKUNDE

President: Dr. G. J. Huët, 39 Brediusweg, Bussum.
Secretary: Dr. H. Reerkink, % Sophia Kinderziekenhuis, 160 Gordelweg, Rotterdam.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

See Medical Association of Israel, National Pediatric Society.

PEDIATRIC SOCIETY OF NEW ZEALAND

President: Dr. Lawrence Ludbrook, The Lister Building, Victoria Street East, Auckland.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASES IN CHILDREN

President: W. W. Payne.
Secretary: Dr. R. E. Bonham Carter; Dr. I. M. Anderson, 52 Harley St., London.
Place: 1 Wimpole St., London W. 1. Time: Fourth Friday of each month, 4:15 p. m.

SCHWEIZERISCHE GESELLSCHAFT FÜR PÄDIATRIE

President: Prof. Dr. A. Hottinger, Petersplatz 12, Basel.
Secretary: Dr. F. Hauser, Kinderspital, Basel.

SOCIEDAD BOLIVIANA DE PEDIATRIA

President: Dr. Carlos Ferrufino, Casilla 272, La Paz, Bolivia.
Secretary: Dr. Cecilio Abela D., Casilla 272, La Paz, Bolivia.
Place: S. C. I. S. P. Bldg. Time: Every Thursday.

SOCIEDAD CHILENA DE PEDIATRIA

Chairman: Dr. Jose Bauza.
Secretary: Dr. Guillermo Llodra, Merced 565, Santiago, Chile.
Place: Medical Society, Merced 565, Santiago, Chile. Time: 7 p. m., every Thursday.

SOCIEDAD CUBANA DE PEDIATRIA

President: Prof. Agustin Castellanos.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: 9 p. m., last Wednesday of every month.

SOCIEDAD DOMINICANA DE PEDIATRIA

President: Dr. Jaime Jorge, Jose Joaquin Perez, no. 25, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Alberto Peguero, V., Ave. Bolivar 113, P. O. Box, 464, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Friday of every month.

SOCIEDAD ECUATORIANA DE PEDIATRIA

President: Dr. Alfredo Ceballos Carrión.
Secretary: Dr. Rafael Compte Andrade, P. O. Box 3480, Guayaquil.
Place: Hospital Central. Time: 11:30 a. m., every Friday.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jesus Avarez de los Cobos.
Secretary: Dr. Luis Torregrosa F.
Place: Hospital Infantil. Time: Last Thursday of every month.

SOCIEDAD DE PEDIATÍA DE CONCEPCIÓN (CHILE)

President: Dr. Raúl Ortega A., Hospital Clínico Regional, Concepción.
Secretary: Dr. Fidel Urrutia, Hospital Clínico Regional, Concepción.
Place: Hospital Clínico Regional, Concepción. Time: 7:30 p. m., second Tuesday of every month from April to December, inclusive.

SOCIEDAD DE PEDIATRÍA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Albino F. Dottori, Dean Fumes 2000, Esq. Ocaña (N.), Córdoba, Argentina.
Place: Comite pro Defenso del Niño, Dean Fumes 2000, Córdoba, Argentina.
Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDADE PORTUGUÊSA DE PEDIATRIA

President: Prof. Almeida Garrett.
Secretary-Generale: Dr. Cordeiro Ferreira, Hospital de D. Estefania, Lisbon.

SOCIEDAD URUGUAYA DE PEDIATRIA

President: Dr. Conrado Pelfort.
Secretary: Dr. José M. Portillo.
Place: Club Medico del Uruguay, Avenida Agraciada 1464 (Piso 13), Montevideo.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Lya Imber Coronil.
Secretary: Dr. Guillermo Tovar, P. O. Box 5, Caracas.
Place: Hospital Municipal de Niños, Caracas. Time: Once a month.

SOCIEDAD YUCATECA DE PEDIATRIA

President: Dr. José Lavalle, Yucatan, Mexico.
Secretary: Dr. Francisco Solís, Yucatan, Mexico.
Place: Hospital del Niño, Yucatan, Mexico.

SOCIÉTÉ DE PÉDIATRIE DE MONTRÉAL

President: Dr. Paul Letondal, 370 E. Roy St., Montreal, Quebec, Canada.
Secretary-Treasurer: Dr. Edmond Baril, 301 Carré Saint-Louis, App. 1, Montreal, Quebec, Canada.
Time: First and Third Thursday of each month.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. G. Heuyer, 1 Ave. Emile Deschanel, Paris 7e, France.
Secretary: Dr. Maurice Lamy, 94 rue de Varenne, Paris 7e, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of each month.

SOCIETÉ POLONAISE DE PÉDIATRIE

President: Dr. Jan Bogdanowicz, Dzialdowska 1, Warsaw.
Secretary: Dr. Zofia Leimbach, Mieroslawskiego 9 m.6, Warsaw.

SOUTH AFRICAN PAEDIATRIC ASSOCIATION

Chairman: Dr. Basil Melle, 89 Lister Bldg., 195 Jeppe St., Johannesburg, South Africa.
Secretary-Treasurer: Dr. Seymour Heymann, 17 Lister Bldg., 195 Jeppe St., Johannesburg, South Africa.

SWEDISH ASSOCIATION OF PEDIATRICS

President: Prof. A. Lichtenstein, Crown Princess Louise's Children's Hospital, 30 Polhemsgatan, Stockholm.
Secretary: Dr. K. A. Melin, Färjestadsvägen 16, Ängby.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. C. W. Herlitz, Kungliga Skolöverstyrelsen, Stockholm.
Secretary: Dr. M. d'Avignon, Norrtulls Sjukhus, Stockholm.
Place: Swedish Medical Society, Klara Östra Kyrkogata 10, Stockholm and Pediatric Clinic Upsala. Time: Second Friday of each month (except summer).

VIENNA PEDIATRIC SOCIETY

President: Prof. Dr. A. Solé, Karolinen-Kinderspital, Sobieskigasse 31, Vienna 9.
Secretary: Doz. Dr. Asperger, Universitäts-Kinderklinik, Lazarettgasse 14, Vienna 9.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Woodruff L. Crawford, 321 W. State St., Rockford, Ill.
Secretary: Dr. Margaret Mary Nicholson, 1801 Eye St. N. W., Washington, D. C.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Edward B. Shaw, 384 Post St., San Francisco 8.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Annual Meeting: Place: Chicago. Time: Oct. 14-19, 1950.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Valjean Cooke, 8700 Argyle Ave., St. Louis.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. P. E. Williams, 193 James St. S., Hamilton, Ontario.
Secretary-Treasurer: Dr. R. L. Denton, 1615 Cedar Ave., Montreal.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Henry H. Gordon, 4200 E. 9th Ave., Denver 7, Colo.
Secretary-Treasurer: Dr. Robert Ward, Bellevue Hospital, New York 16.
Place: French Lick, Ind. Time: 1950.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Spencer Snow, 75 S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. Esther Gross, 202 E. South Temple St., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. Henry E. Gallup.
Secretary-Treasurer: Dr. Harry Shwachman, 300 Longwood Ave., Boston.
Time: Four meetings a year. Next meeting, Sept. 28, 1950.

North Pacific Pediatric Society

President: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.
Secretary-Treasurer: Dr. S. Gorham Babson, 303 Medical Arts Bldg., Portland, Ore.

Northwestern Pediatric Society

President: Dr. Paul Bancroft, 909 Sharp Bldg., Lincoln, Neb.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. Joseph Lyday, 227 16th St., Denver 2.
Secretary-Treasurer: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.
Place: Children's Hospital of Denver or the Colorado General Hospital. Time: Monthly from October to June.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Carroll M. Pounders, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Samuel F. Ravenel, 371 N. Elm St., Greensboro, N. C.

Southwestern Pediatric Society

President: Chester I. Mead, 1930 Truxton Ave., Bakersfield, Calif.
Secretary: Dr. Clement H. Molony, 416 N. Bedford Dr., Beverly Hills, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., second Wednesday in January, March, May, September and November.

STATE

Alabama Pediatric Society

President: Dr. W. A. Daniel Jr., 115 S. Union St., Montgomery 5, Ala.
Secretary-Treasurer: Dr. D. B. Monsky, 905 Norman Bridge Rd., Montgomery 6, Ala.

Arizona Pediatric Society

President: Dr. Carl A. Holmes, 1401 N. 7th Ave., Phoenix.
Secretary-Treasurer: Jacob M. Sobol, 607 Heard Bldg., Phoenix.
Place: Phoenix or Tucson. Time: On call.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Alice Potter, 1418 Ninth Ave., San Francisco 22.
Secretary: Dr. Carl Erickson, 595 E. Colorado, Pasadena.

Florida State Pediatric Society

President: Dr. Edgar W. Stephens, 910 Harvey Bldg., West Palm Beach.
Secretary: Dr. Hugh A. Carithers, 2000 Park St., Jacksonville 4.
Place: Concurrent with state association convention and fall meeting.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Howard J. Morrison, 444 Drayton St., Savannah.
Secretary-Treasurer: Dr. J. Harry Lange, 490 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. H. L. F. Locke, 179 Allyn St., Hartford, Conn.
Secretary: Dr. L. W. Minor, 119 Main St., Middletown, Conn.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Eugene T. McEnery, 4458 W. Madison St., Chicago 24.
Secretary: Dr. George L. Drennen, Jacksonville, Ill.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOICETY

President: Dr. Charlotte Fisk, 1201 Equitable Bldg., Des Moines 9.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. William C. Rivenbank, 1448 Louisiana Ave., New Orleans 15.
Secretary-Treasurer: Dr. Bertha Wexler, 3439 Prytania St., New Orleans 15.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, PEDIATRIC SOCIETY

Chairman: Dr. Thurman B. Givan, 115 Remsen St., Brooklyn 2.
Secretary: Dr. Reginald A. Higgons, Port Chester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Waldo E. Nelson, Temple University, Philadelphia 40.
Secretary: Dr. Carl C. Fischer, 100 W. Coulter St., Philadelphia 44.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. H. J. Lewis, 2956 Biddle Ave., Wyandotte.
Secretary: Dr. Robert H. Trimby, 122 W. Hillsdale, Lansing.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Place, Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. George Clark, 1817 Vinton St., Omaha.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: Children's Memorial Hospital. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. Thomas B. Walker, Portsmouth.
Secretary-Treasurer: Dr. Ursula G. Sanders, Concord.

NEW JERSEY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Israel J. Wolf, 231 E. 31st St., Paterson.
Secretary: Dr. N. T. Crane, 147 E. 7th St., Plainfield, N. J.

NEW MEXICO STATE PEDIATRIC SOCIETY

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Jean Craven, 19 W. Third St., Lexington, N. C.
Secretary-Treasurer: Dr. Susan C. Dees, Duke Hospital, Durham, N. C.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. William C. Deamer, 3 Fifth Ave., San Francisco 18.
Secretary: Dr. A. L. Gleason, 1066 Longridge Rd., Oakland 10.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

NORTH DAKOTA PEDIATRIC SOCIETY

President: Dr. R. E. Dyson, Northwest Clinic, Minot, N. D.
Secretary-Treasurer: Dr. William J. Ball, Northwest Clinic, Minot, N. D.
Place: Fargo Clinic, Fargo, N. D. Time: October 15.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

PHILIPPINE PEDIATRIC SOCIETY

President: Dr. Alberto V. Tupas, Philippine General Hospital, Manila, Philippines.
Secretary: Dr. Artemio P. Jongco, Philippine General Hospital, Manila, Philippines.
Place: Philippine General Hospital. Time: Every two months.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. B. Owen Ravenel, 95 Rutledge Ave., Charleston 16.
Secretary-Treasurer: Dr. John R. Harvin, 206 N. Sumter St., Sumter.

TENNESSEE PEDIATRIC SOCIETY

President: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Secretary-Treasurer: Dr. C. Barton Etter, 1678 Peach, Memphis 12.
Place: Chattanooga. Time: Second Monday in April.

TEXAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount, Dallas, Texas.
Secretary: Dr. M. C. Carlisle, 1410 Austin Ave., Waco, Texas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. C. P. Brown, 142 W. York St., Norfolk.
Secretary: Dr. E. Berkeley Neal, 303 Washington Ave. S. W., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Thomas G. Folsom, 1139 Fourth Ave., Huntington.
Secretary: Dr. Warren J. Parsons, 425 Eleventh St., Huntington.

WISCONSIN STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.
Secretary: Dr. L. M. Simonson, 1001 N. 8th St., Sheboygan.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. John Hart Davis, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Francis F. Silver, 9400 Euclid Ave., Cleveland.
Place: Allen Memorial Medical Library. Time: 8:15 p. m., October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. A. L. Chute, 170 St. George St., Toronto, Canada.
Secretary: Dr. John Fletcher, 262 St. Clair St. W., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

BALTIMORE CITY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. J. Edmund Bradley, University Hospital, Baltimore 1.
Secretary: Dr. Wilson Grubb, 4 E. 33rd St., Baltimore 18.

BRONX PEDIATRIC SOCIETY

President: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Secretary: Dr. George Weiss, 790 Grand Concourse, New York 51.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Secretary: Dr. Stanley S. Lamm, 20 Plaza St., Brooklyn 17.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, October and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. T. Wood Clarke, 7 Cottage Place, Utica, N. Y.
Secretary-Treasurer: Dr. Fred W. Bush, 11 N. Goodman St., Rochester, N. Y.
Place: Various cities in New York. Time: Third Tuesday of April and October.

Central Ohio Pediatric Society

President: Dr. E. H. Baxter, 327 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. E. V. Turner, 2479 E. Main St., Columbus, Ohio.
Place: As announced. Time: On call.

Chicago Pediatric Society

President: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Secretary: Dr. Alfred S. Traisman, 6349 N. Clark St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. John H. Hunt, Kemper Lane Bldg., Cincinnati.
Secretary: Dr. William F. Hunting, 6048 Montgomery, Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Guy Hacker, 5711 Goliad St., Dallas.
Secretary-Treasurer: Dr. George R. Branch, 4325 Cole Ave., Dallas.
Place: Children's Hospital of Texas and Bradford Memorial Hospital. Time: 1 p. m., third Saturday and 8:30 p. m., the first Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wilfred D. H. Nolting, 16840 E. Warren, Detroit.
Secretary: Dr. Ruben Meyer, 938 Maccabees Bldg., Detroit.
Place: Variable. Time: Five times annually.

Fort Worth Pediatric Society

President: Dr. Frank Cohen, 712 S. Henderson, Fort Worth, Texas.
Secretary: Dr. H. H. Womack, 1422 Pennsylvania, Fort Worth, Texas.
Place: Welch and West Restaurant. Time: Third Friday of each month.

Honolulu Pediatric Society

President: Dr. F. D. Nance, Medical Group, Honolulu.
Secretary-Treasurer: Dr. Teruo Yoshina, 1221 Victoria St., Honolulu.
Place: At doctors' homes in rotation. Third Thursday of each month, 6 p. m.

Houston Pediatric Society

President: Dr. Edward O. Fitch, 3720 Fannin St., Houston, Texas.
Secretary: Dr. Thomas J. Donovan, 3506 Sunset Blvd., Houston 5, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., last Tuesday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Hoel Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

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Secretary: Dr. John Eggleston, Oak Ridge Hospital, Oak Ridge, Tenn.

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President: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Association Bldg., 1025 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

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President: Dr. Samuel Silber, 865 Park Place, Brooklyn.
Secretary: Dr. Jacob J. Lichterman, 1433 Union St., Brooklyn 13.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. John Washington, 2032 Belmont Rd. N. W., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S. E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: Spring and fall.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. C. Barton Etter, 1678 Peach, Memphis 12, Tenn.
Secretary-Treasurer: Dr. Jacob Danciger, 188 S. Bellevue Blvd., Memphis 4, Tenn.
Place: University Center, 4 S. Dunlap. Time: 7 p. m., second Tuesday of every month.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. James Conway, 1721 E. Lake Bluff Blvd., Milwaukee 11, Wis.
Secretary-Treasurer: Dr. Walter Polacheck, 425 E. Wisconsin Ave., Milwaukee 2, Wis.
Place: City Club of Milwauk Time: Second Wednesday in February, April, June, October and December.

NASHVILLE PEDIATRIC SOCIETY

President: Dr. John M. Lee, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Dan S. Sanders Jr., 2103 Hayes St., Nashville, Tenn.
Time: Third Thursday of every month.

NEW YORK ACADEMY OF MEDICINE, SECTION ON PEDIATRICS

Chairman: Dr. John Dorsey Craig, 120 E. 75th St., New York 21.
Secretary: Dr. Morris Greenberg, 143 W. 87th St., New York.
Place: New York Academy of Medicine, 2 E. 103rd St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

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President: Dr. Bertha M. Levy, 717 N. W. 22d St., Oklahoma City 3.
Secretary: Dr. C. M. Bielstein, 301 N. W. 12th St., Oklahoma City 3.
Place: Oklahoma Club. Time: On call.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. D. Stewart Polk, W. Montgomery Ave., Rosemont, Pa.
Secretary: Dr. F. H. Harvie, 133 S. 36th St., Philadelphia 4.
Place: College of Physicians, 19 S. 22nd St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. J. A. Gilmartin, 3708-15th Ave., Pittsburgh.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Municipal Hospital, Pittsburgh. Time: Second Friday in October, December, February and April.

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President: Dr. Harold T. Vogel, 34-20, 86 St., Jackson Heights, N. Y.
Secretary: Dr. Moe Goldstein 111-32, 76th Ave., Forest Hills, L. I.
Place: Forest Hills, N. Y. Time: Third Monday of October 1950, February and April 1951, and first Monday of December 1950.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Thomas S. Chalkley, 421 W. Grace St., Richmond 20, Va.
Secretary-Treasurer: Dr. John Paul Jones, 810 W. Franklin St., Richmond 20, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

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President: Dr. Jerome Glaser, 85 San Gabriel Dr., Rochester 10, N. Y.
Secretary-Treasurer: Dr. Daniel B. Peeler, 1162 Lake Ave., Rochester 13, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

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President: Dr. Merl J. Carson, 500 S. Kingshighway, St. Louis.
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Place: Hotel Branscome. Time: Second Thursday of each month from October to May, inclusive, 6:30 p. m.

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President: Dr. Lucius Hill, 328 Medical Arts Bldg., San Antonio 5.
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Place: Bexar County Medical Library. Time: 7:30 p. m., first Tuesday of every month.

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President: Dr. David M. Harris, Medical Arts Bldg., Seattle 1.
Secretary: Dr. William A. Jaquette Jr., 1305 Seneca, Seattle 1.
Place: College Club. Time: Fourth Friday of each month from September to June at 6:30 p. m.

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Secretary: Dr. J. M. Garrett, 1408 Austin Ave., Waco, Texas.
Place: Providence Hospital, 1725 Colcord, Waco, Texas. Time: Third Thursday of each month.

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President: Dr. Harry W. Kaessler, 147 Prospect Ave., Mount Vernon, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: The Roger Smith Hotel, White Plains, N. Y. Time: Fourth Thursday of every other month from September to June (dinner meetings).

WICHITA PEDIATRIC SOCIETY

President: Dr. Walter L. Schafer, 401 N. Emporia St., Wichita 2, Kan.
Secretary: Dr. William F. McGuire, 401 N. Emporia St., Wichita 2, Kan.
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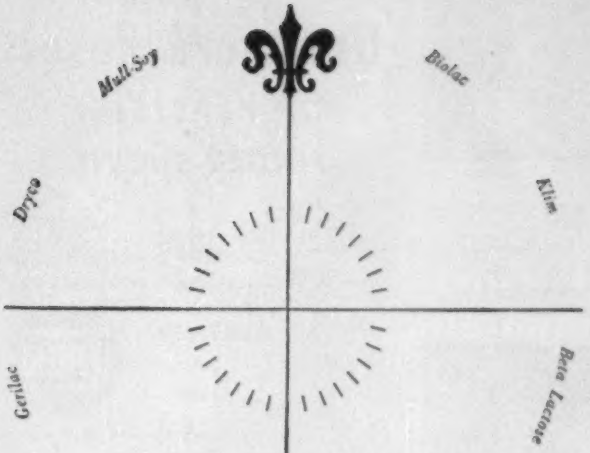

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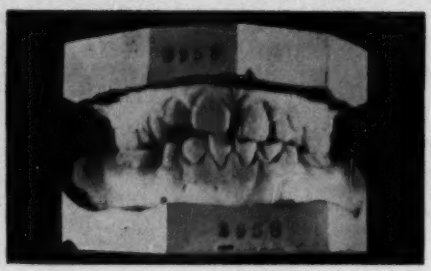

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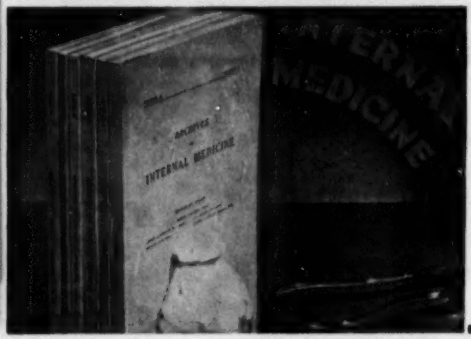

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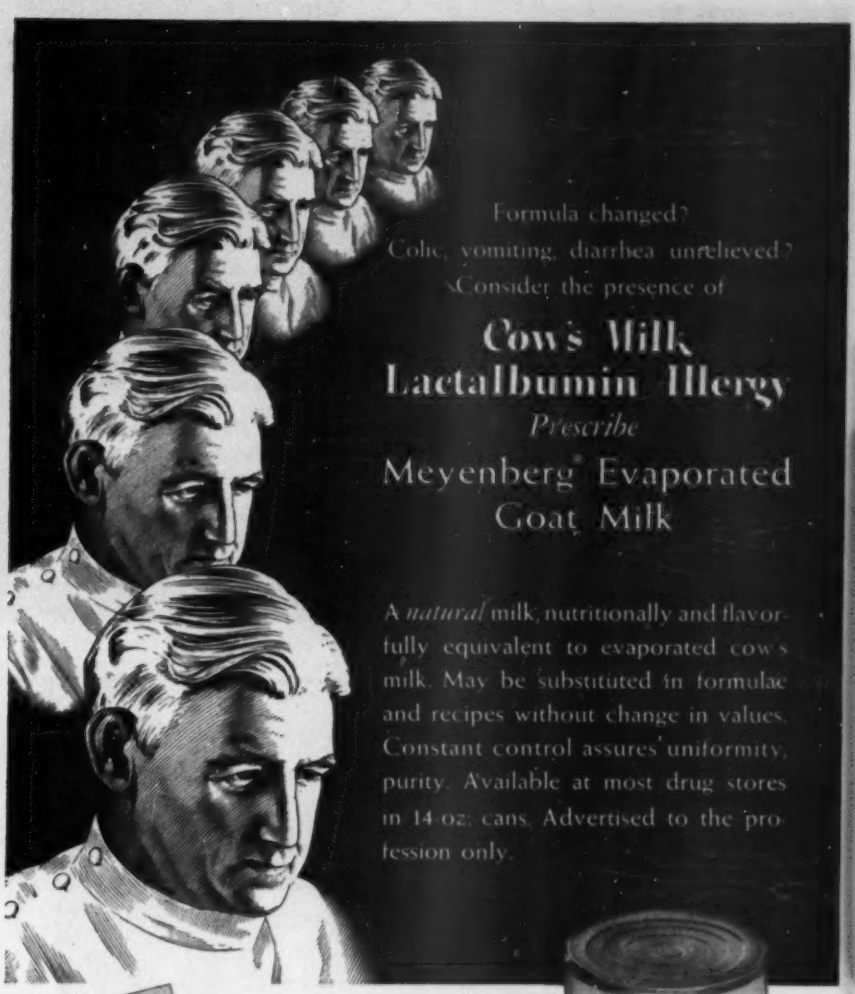

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